



Ex. 13

Ex. 15

Ex. 17

Ex. 26

Ex. 30

Ex. 33

Ex. 34

Ex. 35

Ex. 36

Ex. 38

Ex. 43

Ex. 44

Ex. 45

Ex. 46

Ex. 49

loomada.lezyol

TsO[⊖] (-)-form

Ex. 67

·10025606 ... 22701

Ex. 73

Ex. 75

Ex. 77

Ex. 79

Ex. 72

Ex. 74

Ex. 76

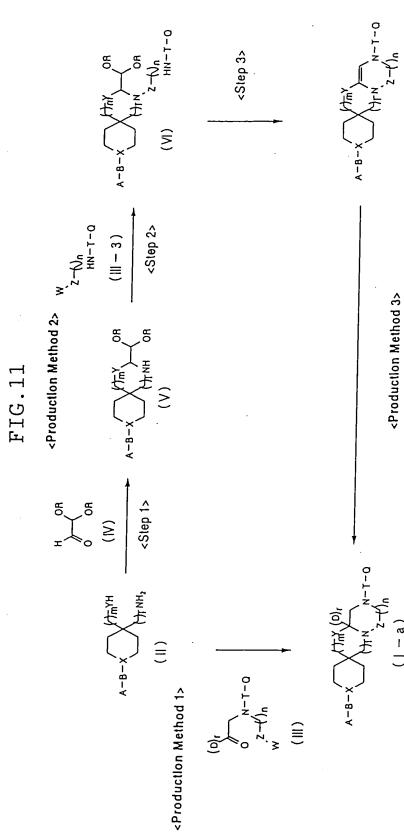
Ex. 78

locesos lezzol

FIG.10

 $Compound \ C$

1002505 .lezyol



10025605.122701

 $\begin{array}{c} \text{Production Method 4} \\ \text{Wethous Method 4} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Wethous Method 4} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Wethous Method 4} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Wethous Method 4} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Cill K} \\ \text{Method 4} \\ \text{Cill K} \\$

	APPROVED O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN	517	7

<Pre><Production Method 1>

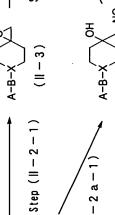
$$A-B-X$$

$$A+B-X$$

$$A+B-$$

<Pre><Pre>cProduction Method 1>

Production Method of (II)



Step (II - 2a - 2)

Step (11 - 3 - 2)

Step (11-3-3)

O.G. FIG.
CLASS SUBCLASS
SIGNATURE 250 APPROVED BY DRAFTSMAN

Production Method of (II) <Pre><Pre>cProduction Method 1>

Y=N

(P-II)

(11-11)

(II – c)

| | OVED O.G. FIG. | |
|-----------|----------------|----------|
| BY | CLASS | SUBCLASS |
| DRAFTSMAN |), , | ~ |

FIG. 15B

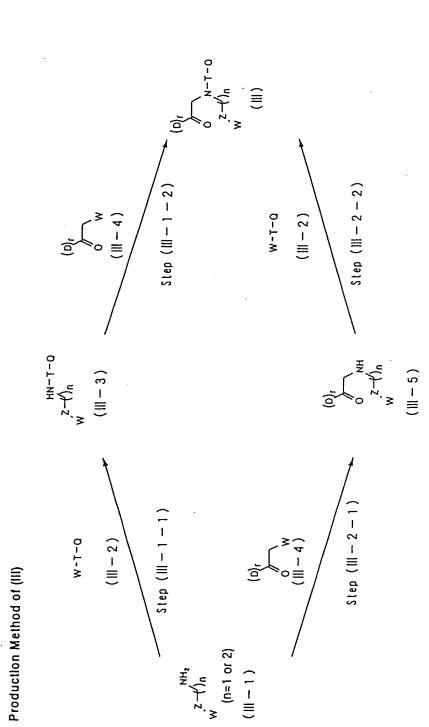
<Production Method 1>
Pr duction Method of (II)
1-2)|=0,1,2 m=1,2

Step (II - 7 - 3) A-B-X NH₂ Step (II - 7 - 2) A-B-X NH₂ Step (II - 6 - 2) (11 - 16)Step (II - 8 - 2) A-B-X OH Step (II -6-1) Step (II - 7 - 1) A-B-X Step (II - 6 - 3) (11 – 13) (11 – 15) Step (II - 8 - 1) (11 - 2)(||-1)

| APPROVED | O.G. FIG. | |
|-----------|-----------|----------|
| BY | CLASS | SUBCLASS |
| DRAFTSMAN | 514 | 28 |

FTG. 16

<Pre><Production Method 1>



<Step 3> $\widehat{\mathbb{S}}$ (111 – 3) <Step 2> (N) 其 <Step 1> <Pre><Production Method 2>

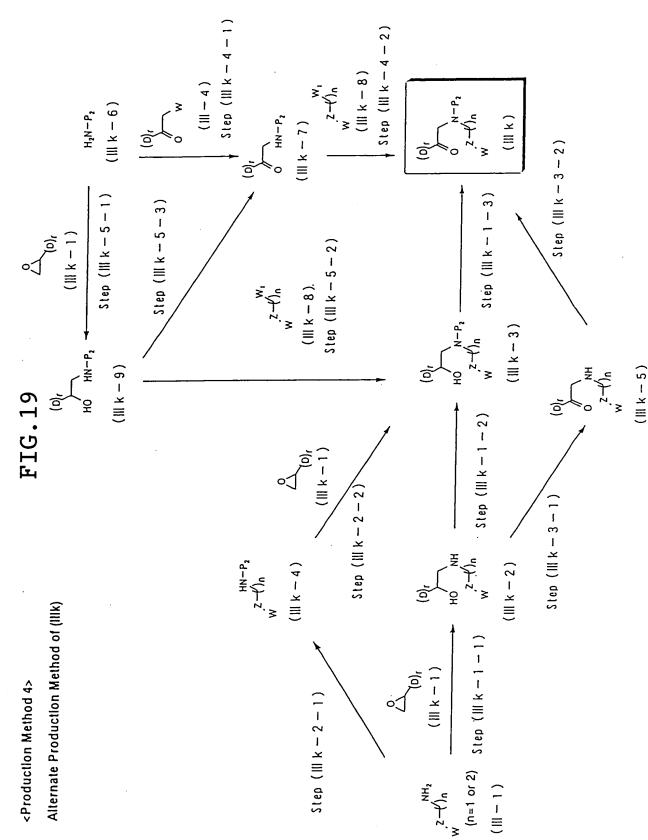
<Pre><Production Method 3>

$$(1-b)$$

locasos larzol

N=X

10026606 1122701



loomede .leevol

| APPROVED | O.G. FIG. | |
|-----------|-----------|----------|
| BY | CLASS | SUBCLASS |
| DRAFTSMAN | SIL | 250 |

$$(-B-x)$$

$$(\int_{T} h dt) \int_{T} h dt$$

$$(\int_{D} h dt)$$

$$(\int_{T} h dt)$$

$$(\int_{T} h dt)$$

$$(\int_{T} h dt)$$

<Converted Example of D (-CH2OH)>

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN S.W. 25

| Ex. No. | (* . JUUMI12/ |
|---------|---|
| 1 | CDCI ₃ *:8.38-8.33 (1H, m), 8.27-8.20 (2H, m), 7.99-7.92 (3H, m), 7.79 (1H, dd, J=2, 9Hz), 7.65-7.59 (1H, m), 6.66-6.58 (2H, m), 4.42-4.32 (2H, m), 4.25-4.17 (1H, m), 3.71-3.58 (2H, m), 3.53-3.17 (5H, m), 3.43 (3H, s), 3.35 (1H, d, J=17Hz), 2.30 (1H, d, J=12Hz), 2.03-1.80 (2H, m), 1.57-1.45 (2H, m) |
| 2 | CDC1 ₃ :8.56 (1H, s), 8.38-8.33 (1H, m), 8.18 (1H, d, J=6Hz), 7.99-7.92 (3H, m), 7.82-7.76 (1H, m), 7.65-7.58 (1H, m), 6.50-6.45 (1H, m), 4.42-4.30 (2H, m), 4.20 (1H, d, J=12Hz), 3.94-3.37 (4H, m), 3.68 (1H, d, J=10Hz), 3.63 (1H, d, J=10Hz), 3.22 (1H, d, J=12Hz), 2.31 (1H, d, J=12Hz), 2.02-1.72 (2H, m), 1.53-1.43 (2H, m) |
| 3 | CDCI ₃ :8.38-8.34 (1H, m), 8.28-8.19 (2H, m), 7.98-7.92 (3H, m), 7.82-7.76 (1H, m), 7.62 (1H, dd, J=2, 9Hz), 6.66-6.58 (2H, m), 4.48-4.22 (3H, m), 3.98-3.88 (1H, m), 3.80-3.69 (1H, m), 3.54-3.15 (5H, m), 3.40 (1H, d, J=17Hz), 2.33 (1H, d, J=12Hz), 2.22-1.82 (2H, m), 1.58-1.48 (2H, m) |
| 4 | CDCI ₃ *:8.37-8.32 (1H, m), 8.28-8.21 (2H, m), 7.99-7.91 (3H, m), 7.78 (1H, dd, J=2, 9Hz), 7.62 (1H, dd, J=2, 9Hz), 6.65-6.58 (2H, m), 4.42-4.10 (7H, m), 3.92 (1H, d, J=10Hz), 3.57-3.16 (6H, m), 2.32 (1H, d, J=12Hz), 2.17-2.06 (1H, m), 1.96-1.83 (1H, m), 1.56-1.47 (2H, m), 1.35-1.20 (3H, m) |
| 5 | CD ₃ 0D:8.53-8.47 (1H, m), 8.18-8.03 (5H, m), 7.92-7.83 (1H, m), 7.68-7.62 (1H, m), 7.18-7.09 (2H, m), 4.34 (1H, d, J=12Hz), 4.35-4.20 (1H, m), 4.20-3.26 (11H, m), 2.65 (1H, d, J=12Hz), 2.22-2.10 (1H, m), 2.02-1.88 (1H, m), 1.73-1.55 (2H, m) |
| 6 | CDC1 ₃ *:8.40-8.37 (1H, m), 8.28-8.20 (2H, m), 8.07-7.93 (3H, m), 7.80-7.64 (3H, m), 6.66-6.58 (2H, m), 4.42-4.30 (2H, m), 4.20 (1H, d, J=12Hz), 3.72-3.61 (2H, m), 3.52-3.18 (4H, m), 3.44 (3H, s), 3.35 (1H, d, J=17Hz), 3.21 (1H, d, J=12Hz), 2.28 (1H, d, J=12Hz), 2.04-1.79 (2H, m), 1.57-1.45 (2H, m) |
| 7 | CDC1 ₃ *:8.40-8.36 (1H, m), 8.29-8.20 (2H, m), 8.00-7.94 (3H, m), 7.80 (1H, dd, J=2, 9Hz), 7.63 (1H, dd, J=2, 9Hz), 6.66-6.59 (2H, m), 4.54-4.15 (5H, m), 3.60-3.14 (6H, m), 2.36 (1H, d, J=12Hz), 2.13 (3H, s), 1.99-1.73 (2H, m), 1.62-1.46 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN S IM 25

FIG.22

| | (27011) |
|---------|--|
| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
| 8 | CDCI ₃ *:8.37-8.34 (1H, m), 8.26-8.19 (2H, m), 7.99-7.91 (3H, m), 7.79 (1H, dd, J=2, 9Hz), 7.65-7.59 (1H, m), 6.62-6.55 (2H, m), 4.72 (1H, dd, J=2, 14Hz), 4.35-4.25 (2H, m), 4.07 (1H, d, J=11Hz), 3.74 (1H, d, J=12Hz), 3.63 (1H, d, J=11Hz), 3.49 (3H, s), 3.34 (1H, d, J=17Hz), 3.63-3.28 (3H, m), 3.26-3.11 (2H, m), 2.68 (1H, d, J=14Hz), 2.42 (1H, d, J=12Hz), 1.68-1.40 (4H, m) |
| 9 | CDC1 ₃ :8.45-8.13 (3H, m), 8.00-7.90 (3H, m), 7.79 (1H, dd, J=2, 8Hz), 7.62 (1H, dd, J=2, 9Hz), 6.82-6.58 (2H, m), 5.26-5.18 (1H, m), 4.45-4.26 (2H, m), 3.77 (1H, d, J=12Hz), 3.70-3.51 (2H, m), 3.47-3.23 (2H, m), 3.32 (1H, d, J=17Hz), 3.19 (1H, d, J=12Hz), 2.52-2.39 (1H, m), 2.06-1.88 (1H, m), 1.85-1.59 (3H, m) |
| 10 | CDCI ₃ *:8.59 (1H, s), 8.40-8.35 (1H, m), 8.20 (1H, d, J=6Hz), 8.04-7.87 (3H, m), 7.80 (1H, dd, J=2, 9Hz), 7.61 (1H, dd, J=2, 9Hz), 6.52 (1H, d, J=6Hz), 5.27-5.18 (1H, m), 4.45-4.28 (2H, m), 4.12-3.94 (2H, m), 3.81-3.71 (1H, m), 3.55-3.32 (2H, m), 3.32 (1H, d, J=17Hz), 3.23-3.15 (1H, m), 2.46 (1H, dd, J=9, 12Hz), 2.01-1.88 (1H, m), 1.79-1.60 (3H, m) |
| 11 | CDCI ₃ *:8.31-8.25 (2H, m), 7.50 (1H, d, J=15Hz), 7.49-7.38 (4H, m), 6.72-6.60 (3H, m), 5.23-5.17 (1H, m), 4.33-4.22 (2H, m), 3.87-3.80 (1H, m), 3.65-3.51 (2H, m), 3.59 (1H, d, J=17Hz), 3.44-3.27 (2H, m), 3.25-3.19 (1H, m), 2.78-2.69 (1H, m), 2.02-1.92 (1H, m), 1.88-1.69 (3H, m) |
| 12 | CDCI ₃ :14.2 (1H, brs), 8.40-8.33 (1H, m), 8.28-8.15 (2H, m), 8.02-7.92 (3H, m), 7.83-7.75 (1H, m), 7.67-7.58 (1H, m), 6.94-6.82 (2H, m), 4.45-4.26 (2H, m), 4.26-4.13 (1H, m), 3.96-3.23 (8H, m), 3.43 (3H, s), 2.86 (3H, s), 2.34 (1H, d, J=12Hz), 2.18-2.04 (1H, m), 1.96-1.79 (1H, m), 1.68-1.54 (2H, m) |
| 13 | CDCl ₃ :14.21 (1H, brs), 8.40-8.33 (1H, m), 8.28-8.15 (2H, m), 8.02-7.92 (3H, m), 7.83-7.75 (1H, m), 7.67-7.58 (1H, m), 6.94-6.82 (2H, m), 4.45-4.26 (2H, m), 4.26-4.13 (1H, m), 3.96-3.23 (8H, m), 3.43 (3H, s), 2.86 (3H, s), 2.34 (1H, d, J=12Hz), 2.18-2.04 (1H, m), 1.96-1.79 (1H, m), 1.68-1.54 (2H, m) |
| 14 | CD ₃ OD:8.53-8.48 (1H, m), 8.16-8.03 (5H, m), 7.91-7.85 (1H, m), 7.66 (1H, dd, J=2, 9Hz), 7.18-7.08 (2H, m), 4.32-4.12 (3H, m), 4.08-3.96 (1H, m), 3.94-3.60 (4H, m), 3.58-3.42 (1H, m), 3.50 (1H, d, J=17Hz), 3.38-3.27 (1H, m), 2.69 (3H, s), 2.62 (1H, d, J=12Hz), 2.13-1.85 (2H, m), 1.72-1.53 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

SIMPLE OF THE PROPERTY OF THE PROPERTY

| Ex. No. | NMR (270MHz) (ppm) |
|---------|---|
| EX.NU. | |
| 15 | DMS0- d_6 :13.32-13.10 (1H, br), 8.61 (1H, s), 8.34-8.12 (5H, m), 7.95-7.86 (1H, m), 7.79-7.70 (1H, m), 7.24-7.14 (2H, m), 4.22-4.03 (6H, m), 3.94-2.90 (9H, m), 2.71 (1H, d, J=11Hz), 2.30 (3H, s), 1.97-1.81 (2H, m), 1.64-1.49 (2H, m), 1.26-1.16 (3H, m) |
| 17 | CDCl ₃ :8.40-8.35 (1H, m), 8.30-8.21 (2H, m), 8.00-7.92 (3H, m), 7.82-7.76 (1H, m), 7.65-7.59 (1H, m), 6.93-6.85 (2H, m), 5.28-5.20 (1H, m), 4.44-4.32 (1H, m), 4.33 (1H, d, J=17Hz), 4.00-3.80 (3H, m), 3.65-3.40 (2H, m), 3.34 (1H, d, J=17Hz), 3.21 (1H, d, J=12Hz), 2.85 (3H, s), 2.58-2.47 (1H, m), 3.20-1.70 (4H m) |
| 20 | CDC1 ₃ *:8.37-8.33 (1H, m), 8.28-8.20 (2H, m), 7.98-7.92 (3H, m), 7.81-7.75 (1H, m), 7.65-7.59 (1H, m), 6.65-6.59 (2H, m), 4.40-4.28 (2H, m), 4.17 (1H, d, J=11Hz), 3.83-3.73 (2H, m), 3.72-3.66 (2H, m), 3.59-3.53 (2H, m), 3.38 (3H, s), 3.51-3.22 (6H, m), 2.31 (1H, d, J=12Hz), 2.09-1.98 (1H, m), 1.93-1.80 (1H, m), 1.54-1.46 (2H, m) |
| 21 | DMSO- $d_6*:13.34-13.12$ (1H, br), 8.62 (1H, s), 8.34-8.25 (2H, m), 8.24-8.13 (3H, m), 7.96-7.87 (1H, m), 7.79-7.72 (1H, m), 7.24-7.16 (2H, m), 4.18-4.02 (3H, m), 3.94-3.80 (1H, m), 3.80-3.68 (1H, m), 3.26 (3H, s), 3.68-3.15 (10H, m), 2.70 (1H, d, J=11Hz), 2.30 (3H, s), 1.94-1.81 (2H, m), 1.64-1.51 (2H, m) |
| 22 | CDC1 ₃ *:8.37-8.34 (1H, m), 8.27-8.21 (2H, m), 7.99-7.92 (3H, m), 7.81-7.76 (1H, m), 7.65-7.60 (1H, m), 6.64-6.58 (2H, m), 4.55-4.48 (1H, m), 4.39 (1H, d, J=17Hz), 4.25 (1H, d, J=12Hz), 3.88 (1H, d, J=10Hz), 3.85-3.72 (3H, m), 3.72-3.60 (2H, m), 3.50-3.42 (2H, m), 3.34 (1H, d, J=17Hz), 3.42-3.23 (2H, m), 3.18 (1H, d, J=12Hz), 2.27 (1H, d, J=12Hz), 2.02-1.80 (2H, m), 1.56-1.46 (2H, m) |
| 23 | CDC ₁₃ *:8.37-8.33 (1H, m), 8.22-8.14 (2H, m), 7.99-7.92 (3H, m), 7.80-7.71 (3H, m), 7.60 (1H, dd, J=2, 9Hz), 7.15-7.07 (4H, m), 4.38-4.26 (2H, m), 4.13 (1H, d, J=12Hz), 3.96 (3H, s), 3.95-3.80 (2H, m), 3.65 (2H, s), 3.41 (3H, s), 3.63-3.35 (2H, m), 3.35 (1H, d, J=17Hz), 3.23 (1H, d, J=12), 2.35 (1H, d, J=12Hz), 2.31 (3H, s), 2.09-1.99 (1H, m), 1.90-1.76 (1H, m), 1.60-1.50 (2H, m) |
| 24 | CDC1 ₃ *:8.36-8.31 (1H, m), 8.26-8.18 (2H, m), 7.98-7.90 (3H, m), 7.81-7.75 (1H, m), 7.63-7.56 (1H, m), 6.66-6.59 (2H, m), 3.81-3.72 (1H, m), 3.63 (1H, d, J=11Hz), 3.40 (3H, s), 3.50-3.22 (7H, m), 3.10-3.01 (1H, m), 2.97-2.84 (2H, m), 2.77-2.66 (1H, m), 2.25 (1H, d, J=12Hz), 2.01-1.90 (1H, m), 1.76-1.59 (3H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

GIASTSMAN SIGNATURE CONTROL CON

FIG.24

| | NMR (270MHz) (ppm) |
|---------|--|
| Ex. No. | (*:300MHz) |
| | CDC1 ₃ :8.35 (1H, s), 8.30-8.20 (2H, m), 8.00-7.86 (3H, |
| | m), 7.82-7.71 (1H, m), 7.66-7.56 (1H, m), 6.66-6.57 |
| | (2H, m), 4.76 (1H, d, J=12Hz), 4.38-4.21 (3H, m), 4.11 |
| 0.5 | (1H, d, J=12Hz), 3.54-3.23 (6H, m), 2.49 (1H, d, |
| 25 | J=12Hz), 1.89-1.73 (2H, m),
1.73-1.52 (2H, m), 1.41-1.29 (3H, m) |
| | CDCI ₃ :14.43 (1H, brs), 8.36 (1H, s), 8.28-8.16 (2H, |
| | m), 8.02-7.86 (3H, m), 7.82-7.73 (1H, m), 7.66-7.57 |
| | (1H, m), 6.97-6,88 (2H, m), 4.82-4.70 (1H, m), 4.40- |
| | 4.21 (3H, m), 4.14 (1H, d, J=12Hz), 3.95-3.80 (2H, m), |
| 26 | 3.66-3.29 (4H, m), 2.82 (3H, s),
2.58-2.48 (1H, m), 1.98-1.77 (2H, m), 1.77-1.63 (2H, |
| | m) 1 44-1 30 (3H, m) |
| | $DMSO-d_6*:8.60$ (1H, s), 8.30 (1H, d, J=9Hz), 8.27-8.21 |
| | (1H, m), 8.21-8.08 (3H, m), 7.94-7.84 (1H, m), 7.77- |
| | 7.69 (1H, m), 6.99 (2H, d, J=7Hz), 4.48 (1H, d, |
| . 07 | J=11Hz), 3.98-3.82 (2H, m), 3.76-3.54 (2H, m), 3.54-3.17 (2H, m), 3.39 (1H, d, J=16Hz), |
| 27 | 3.23 (1H, d, J=12Hz), 2.71 (1H, d, J=11Hz), 1.79-1.64 |
| | (2H m) 1 64-1 47 (2H m) |
| | $CDC1_3*:8.42-8.32$ (1H, m), 8.31-8.18 (2H, m), 8.02-7.88 |
| | (3H, m), 7.83-7.73 (1H, m), 7.67-7.57 (1H, m), 6.70- |
| | 6.58 (2H, m), 4.80-4.68 (1H, m), 4.33 (1H, d, J=17Hz), 4.13 (1H, d, J=12Hz), 3.82 (3H, s), 3.56-3.25 (6H, m), |
| 28 | 2.57-2.47 (1H, m), 2.04-1.54 (4H, m) |
| | |
| | CDC1 ₃ *:8.39-8.31 (1H, m), 8.31-8.18 (2H, m), 8.00-7.88 |
| | (3H, m), 7.86-7.75 (1H, m), 7.65-7.58 (1H, m), 6.64 (2H, d, J=7Hz), 5.22-5.07 (1H, m), 4.80-4.72 (1H, m), |
| | 4. 36-4. 25 (1H, m), 4. 07 (1H, d, J=11Hz), 3. 57-3. 25 |
| 29 | (6H, m), 2.46 (1H, d, J=11Hz), |
| | 1.88-1.72 (2H, m), 1.72-1.50 (2H, m), 1.39 (3H, d, |
| | J=6Hz), 1.34 (3H, d. J=6Hz) |
| | $CDCI_3*:8.39-8.32$ (1H, m), $8.31-8.18$ (2H, m), $8.00-7.88$ (3H, m), $7.82-7.74$ (1H, m), $7.66-7.57$ (1H, m), $6.70-$ |
| | 6.55 (2H, m), 4.83-4.70 (1H, m), 4.32 (1H, d, J=17Hz), |
| | 4.25-4.05 (3H, m), 3.58-3.23 (6H, m), 2.55-2.44 (1H, |
| 30 | $ m\rangle$, 2.00-1.50 (6H, $m\rangle$, |
| | 1.05-0.93 (3H, m)
CDC1 ₃ *:8.36 (1H, s), 8.32-8.17 (2H, m), 8.04-7.85 (3H, |
| | $(1000)_3$ = 18.36 (1H, s), 8.32-8.17 (2H, m), 8.04-7.83 (3H, m), 7.83-7.72 (1H, m), 7.68-7.56 (1H, m), 6.70-6.55 |
| | (2H, m), 6.05-5.85 (1H, m), 5.48-5.26 (2H, m), 4.85- |
| | 4.60 (3H, m), 4.33 (1H, d, J=17Hz), 4.12 (1H, d, |
| 31 | J=12Hz), 3.57-3.20 (6H, m), |
| | 2.51 (1H, d, J=12Hz), 1.90-1.72 (2H, m), 1.72-1.50 |
| | (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

CRAFTSMAN (14) 25

FIG.25

| | 110.25 |
|---------|---|
| Ex. No. | N.M.R (270MHz) (ppm) |
| | (*:300MHz)
CDCI ₃ *:8.36 (1H, s), 8.31-8.18 (2H, m), 8.03-7.87 (3H, |
| | (11, 13), $(11, 13)$, $(11,$ |
| | (2H, m), 4.78(1H, d, J=12Hz), 4.45-4.25 (3H, m), 4.10 |
| | (2H, m), 4.78(H , d, $J=12H2$), 4.43 4.23 (SH , M), 4.10 (SH , SH), 4.10 (SH), SH |
| 32 | 3.57-3.23 (6H, m), 2.51 (1H, d, J=12Hz), |
| 32 | 1. 93-1. 53 (4H, m) |
| | CDC1 ₃ *:8.38-8.32 (1H, m), 8.32-8.20 (2H, m), 8.01- |
| • | 7.91(3H, m), 7.82-7.75 (1H, m), 7.66-7.58 (1H, m), |
| | 6.68-6.60(2H, m), 4.79-4.70 (1H, m), 4.32 (1H, d, |
| | J=17Hz), 4.04 (1H, d, $J=12Hz$), 3.56-3.22 (5H, m), 3.28 |
| 33 | (1H, d, J=17Hz), |
| | 2.42 (1H, d, J=2, 11Hz), 1.92-1.76 (2H, m), 1.70- |
| | 1.48(2H, m), 1.58 (9H, s)
CDCI ₃ *:8.38-8.31 (1H, m), 8.31-8.16 (2H, m), 8.00-7.90 |
| | CDC1 ₃ *:8.38-8.31 (1H, m), 8.31-8.16 (2H, m), 8.00-7.90 |
| | (3H, m), 7.82-7.73 (1H, m), 7.65-7.58 (1H, m), 6.92- |
| | 6.82 (1H, m), 6.70-6.60 (2H, m), 4.80-4.71 (1H, m), 4.39-4.18 (3H, m), 4.14-4.00 (1H, m), 3.64-3.20 (6H, |
| 34 | m), 2.54-2.43 (1H, m), 2.40-1.55 (7H, m), |
| J-4 | 1 40-1 29 (3H m) |
| | $CDC1_3*:8.38-8.34$ (1H, m), 8.30-8.22 (2H, m), 7.99-7.92 |
| | (3H, m), 7.78 (1H, dd, J=2, 9Hz), 7.62 (1H, dd, J=2, |
| | 9Hz , 6,66-6,60 (2H, m), 4.81-4.73 (1H, m), 4.38-4.24 |
| | (3H, m), 4.11 (1H, d, J=12Hz), 3.54-3.24 (6H, m), 2.49 |
| 35(+) | (1H, d, J=12Hz), 1.84-1.77 (2H, m), |
| | 1.67-1.58 (2H, m), 1.36 (3H, t, J=7Hz)
CDCI ₃ *:8.38-8.34 (1H, m), 8.29-8.23 (2H, m), 7.99-7.92 |
| | (3H, m), 7.78 (1H, dd, J=2, 9Hz), 7.62 (1H, dd, J=2, |
| | 9Hz), 6.66-6.60 (2H, m), 4.81-4.73 (1H, m), 4.38-4.24 |
| | (3H, m), 4.11 (1H, d, J=12Hz), 3.54-3.25 (6H, m), 2.49 |
| 35(-) | (1H, d, J=12Hz), 1.84-1.76 (2H, m), |
| | 1 68-1 58 (2H. m), 1.36 (3H. t. J=7Hz) |
| | DMSO-d ₆ *:13.24 (1H, s), 8.64 (1H, s), 8.35-8.20 (5H, |
| | m), 7.95-7.85 (1H, m), 7.76 (1H, dd, J=2, 9Hz), 7.35- |
| | 7.20 (2H, m), 4.50-4.35 (1H, m), 4.25-4.15 (2H, m), |
| 26 | 4.14-4.00 (2H, m), 3.90-3.75 (2H, m), 3.65-3.20 (4H, m), 3.00-2.85 (1H, m), 2.29 (3H, s), |
| 36 | 1.90-1.60 (4H, m), 1.25 (3H, t, J=7Hz) |
| | $DMSO-d_6*:8.61$ (1H, s), 8.30 (1H, d, J=9Hz), 8.27-8.22 |
| | (1H, m), 8.22-8.08 (3H, m), 7.93-7.86 (1H, m), 7.77- |
| | 7.69 (1H. m). 6.98 (2H. d. J=7Hz), 4.54-4.41 (1H, m), |
| | 4.00-3.80 (2H, m), 3.80-3.16 (4H, m), 3.39 (1H, d, |
| 37 | J=16Hz), 3.23 (1H, d, J=12Hz), |
| | 2.75-2.65 (1H, m), 1.80-1.65 (2H, m), 1.65-1.45 (2H, |
| | m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

STATEMENT OF THE PROVED OF T

| | F1G.20 |
|----------|---|
| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
| | CDCI ₃ *:8.39-8.33 (1H, m), 8.30-8.22 (2H, m), 8.00-7.91 |
| | (3H, m), 7.81-7.74 (1H, m), 7.62 (1H, dd, J=2, 9Hz), |
| | 6.67-6.59 (2H. m), 4.80-4.70 (1H, m), 4.33 (1H, d, |
| | J=17Hz), 4.13 (1H, d, $J=11Hz$), 3.82 (3H, s), 3.54-3.24 |
| 38 | (6H, m), 2.56-2.47 (1H, m), |
| | 1 QQ-1 55 (AH m) |
| | CDCI ₃ *:8.36-8.33 (1H, m), 8.30-8.21 (2H, m), 8.00-7.90 |
| | (3H, m), 7.82-7.70 (1H, m), 7.65-7.58 (1H, m), 6.68- |
| | 6.58 (2H, m), 5.22-5.08 (1H, m), 4.82-4.71 (1H, m), |
| | 4. 32 (1H, d, J=17Hz), 4. 07 (1H, d, J=12Hz), 3. 58-3. 23 |
| 39 | (5H, m), 3.39 (1H, d, J=12Hz), |
| | 2.46 (1H, d, J=11Hz), 1.88-1.72 (2H, m), 1.72-1.53 (2H, m), 1.39 (3H, d, J=6Hz), 1.34 (3H, d, J=6Hz) |
| <u> </u> | $CDC1_3 *: 8.39 - 8.32$ (1H, m), 8.30 - 8.20 (2H, m), 8.02 - 7.88 |
| | (3H, m), 7.83-7.73 (1H, m), 7.66-7.57 (1H, m), 6.69- |
| } | [6.57 (2H m)] 4.82-4.73 (1H. m). 4.32 (1H. d. J=17Hz), |
| | 4.24-4.05 (3H, m), 3.58-3.23 (6H, m), 2.55-2.44 (1H, |
| 40 | m), 1.87-1.54 (6H, m), 1.06-0.94 (3H, m) |
| | |
| | CDC1 ₃ *:8.33-8.39 (1H, m), 8.30-8.20 (2H, m), 7.99-7.91 |
| | (3H, m), 7.82-7.73 (1H, m), 7.62 (1H, dd, J=2, 9Hz), |
| ļ | 6.67-6.58 (2H, m), 6.04-5.88 (1H, m), 5.46-5.30 (2H, |
| | m), 4.83-4.63 (3H, m), 4.33 (1H, d, J=17Hz), 4.12 (1H, d, J=12Hz), 3.55-3.22 (6H, m), |
| 41 | 2.51 (1H, d, J=12Hz), 1.85-1.75 (2H, m), 1.70-1.57 |
| | (2H, m) |
| | CDC1 ₃ *:8.38-8.33 (1H, m), 8.30-8.20 (2H, m), 8.00-7.90 |
| | (3H, m), 7.83-7.74 (1H, m), 7.62 (1H, dd, J=2, 9Hz), |
| | 6 67-6 58 (2H, m), 4.83-4.73 (1H, m), 4.42-4.27 (3H, |
| | $ m\rangle$, 4.09 (1H, d, J=12Hz), 3.75-3.58 (2H, m), 3.40 (3H, |
| 42 | s). 3.55-3.22 (6H. m). |
| | 2.55-2.46 (1H, m), 1.92-1.53 (4H, m)
CDCl ₃ *:8.40-8.32 (1H, m), 8.32-8.19 (2H, m), 8.02- |
| | CDC13*:8.40-8.32 (IH, M), 8.32-8.19 (2H, M), 6.02- |
| | 7.89(3H, m), 7.84-7.75 (1H, m), 7.68-7.57 (1H, m), 6.70-6.59 (2H, m), 4.81-4.69 (1H, m), 4.31 (1H, d, |
| | J=17Hz), 4.04 (1H, d, J=12Hz), 3.57-3.20 (5H, m), 3.28 |
| 43 | (1H, d, J=17Hz), 2.48-2.37 (1H, m), |
| 43 | 1, 92-1, 72 (2H, m), 1, 72-1, 45 (2H, m), 1, 58 (9H, m) |
| | CDC1 ₃ *:14.36 (1H, brs), 8.38-8.34 (1H, m), 8.25-8.17 |
| | (2H. m), 8.00-7.93 (3H, m), 7.77 (1H, dd, J=2, 9Hz), |
| | 7.62 (1H, dd, $J=2$, 9Hz), $7.00-6.91$ (2H, m), 4.74 (1H, |
| } | d, J=12Hz), 4.32 (1H, d, J=17Hz), 4.15 (1H, d, |
| 44 | J=12Hz), 3.95-3.80 (2H, m), 3.83 (3H, s), |
| | 3.63-3.35 (4H, m), 2.83 (3H, s), 2.57 (1H, d, J=12Hz), |
| | 1.95-1.78 (2H, m), 1.76-1.66 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN SUBCLASS

FIG.27

| | r IG. Z/ |
|---------|--|
| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
| 49 | CDCI ₃ *:14.22 (1H, brs), 8.38-8.32 (1H, m), 8.27-8.17 (2H, m), 8.00-7.90 (3H, m), 7.82-7.74 (1H, m), 7.62 (1H, dd, J=2, 9Hz), 6.99-6.89 (2H, m), 4.78-4.69 (1H, m), 4.36-4.25 (1H, m), 4.06 (1H, d, J=12Hz) 3.96-3.80 (2H, m), 3.66-3.38 (3H, m), 3.34-3.23 (1H, m), 2.83 (3H, s), 2.51-2.42 (1H, m), 1.99-1.78 (2H, m), 1.75-1.65 (2H, m), 1.58 (9H, s) |
| 50 | CD ₃ OD*:8.47 (1H, s), 8.12 (1H, d, J=9Hz), 8.12-7.99 (4H, m), 7.92-7.83 (1H, m), 7.63 (1H, dd, J=2, 9Hz), 6.82-6.74 (2H, m), 4.65-4.55 (1H, m), 4.14 (1H, d, J=16Hz), 3.89 (1H, d, J=12Hz), 3.68-3.25 (6H, m), 2.72-2.64 (1H, m), 2.02-1.87 (1H, m), 1.82-1.68 (1H, m), 1.68-1.52 (2H, m) |
| 51 (+) | $CD_3OD*:8.49$ (1H, s), 8.23-8.01 (5H, m), 7.88-7.86 (1H, m), 7.70-7.61 (1H, m), 6.89-6.71 (2H, m), 4.65-4.54 (1H, m), 4.20-4.08 (1H, m), 3.89 (1H, d, J=12Hz), 3.69-3.18 (6H, m), 2.78-2.64 (1H, m), 2.00-1.52 (4H, m) |
| 51 (-) | $CD_3OD*:8.48$ (1H, s), 8.12 (1H, d, J=9Hz), 8.16-8.00 (4H, m), 7.94-7.83 (1H, m), 7.67-7.60 (1H, m), 6.86-6.75 (2H, m), 4.63-4.53 (1H, m), 4.12 (1H, d, J=17Hz), 3.89 (1H, d, J=11Hz), 3.69-3.21 (6H, m), 2.74-2.65 (1H, m), 1.97-1.86 (1H, m), 1.81-1.52 (3H, m) |
| 52 | CDCI ₃ *:8.33 (1H, s), 8.24-8.13 (2H, m), 7.99-7.89 (3H, m), 7.80-7.69 (3H, m), 7.59 (1H, dd, J=2, 9Hz), 7.22-7.13 (2H, m), 7.12-7.06 (2H, m), 4.79-4.68 (1H, m), 4.36-4.21 (3H, m), 4.19-4.02 (3H, m), 3.98-3.84 (2H, m), 3.56-3.28 (4H, m), 2.59-2.50 (1H, m), 2.30 (3H, s), 1.87-1.72 (2H, m), 1.70-1.55 (2H, m), 1.46-1.30 (6H, m) |
| 53 | CD ₃ OD:8.52-8.48 (1H, m), 8.16-8.04 (3H, m), 7.88 (1H, dd, J=2, 9Hz), 7.69-7.60 (3H, m), 7.04-6.95 (2H, m), 4.35-4.10 (3H, m), 3.39 (3H, s), 3.68-3.22 (8H, m), 2.58 (1H, d, J=12Hz), 1.98-1.86 (2H, m), 1.62-1.51 (2H, m) |
| 54 | CDCI ₃ *:8.54-8.49 (2H, m), 8.36-8.33 (1H, m), 7.97-7.91 (3H, m), 7.80-7.75 (1H, m), 7.61 (1H, dd, J=2, 9Hz), 7.24-7.19 (2H, m), 4.40-4.30 (2H, m), 4.19 (1H, d, J=12Hz), 3.46 (2H, s), 3.41 (3H, s), 3.68-3.52 (2H, m), 3.32 (1H, d, J=17Hz), 3.12 (1H, d, J=12Hz), 2.66-2.54 (1H, m), 2.52-2.20 (3H, m), 2.25 (1H, d, J=12Hz), 2.00-1.77 (2H, m), 1.54-1.36 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

ORAFTSMAN 5 4 25

FIG.28

| | r 1G. 20 |
|----------|--|
| Ex. No. | NMR (270MHz) (ppm) |
| EX. NO. | (か.3UUMNZ) |
| | CDC1 ₃ *:8.38-8.34 (1H, m), 8.20-7.92 (5H, m), 7.78 (1H, |
| | dd, J=2, 9Hz), 7.62 (1H, dd, J=2, 9Hz), 6.65-6.58 (2H, |
| | m), 4.42-4.30 (2H, m), 4.21 (1H, d, J=12Hz), 3.67 (1H, |
| | d, J=10Hz), 3.63 (1H, d, J=10Hz), 3.43 (3H, s), 3.50- |
| 55 | 3.18 (6H, m), 2.30 (1H, d, J=12Hz), |
| | 2.06-1.80 (2H, m), 1.59-1.50 (2H, m)
CDCI ₃ *:8.37-8.33 (1H, m), 7.98-7.91 (3H, m), 7.81-7.75 |
| | (1H, m), 7.61 $(1H, dd, J=2, 9Hz)$, 4.40-4.30 $(2H, m)$, |
| | 4.19 (1H, d, J=12Hz), $3.69-3.56$ (2H, m), 3.42 (3H, s), |
| | 3.54-3.26 (4H, m), 3.34 (1H, d, J=17Hz), 3.18 (1H, d, |
| 56 | I=12Hz) |
| 30 | 2 06 (3H, s), 1.94-1.72 (2H, m), 1.46-1.38 (2H, m) |
| | 2.06 (3H, s), 1.94-1.72 (2H, m), 1.46-1.38 (2H, m) DMSO-d ₆ (100°C) *:9.04-8.70 (1H, m), 8.56-8.51 (1H, m), |
| | 8.50-8.30 (1H, m), 8.23 (1H, d, J=9Hz), 8.19-8.10 (2H, |
| | m . 7.86 (1H, dd, J=2, 9Hz), 7.71-7.65 (1H, m), 4.16- |
| | 4.03 (3H, m), 3.79-2.44 (9H, m), 3.28 (3H, s), 2.32 |
| 57 | (3H, s), 2.28-2.21 (3H, m), |
| | 1.99-1.84 (2H, m), 1.68-1.58 (2H, m) |
| | CDC1 ₃ :8.39-8.33 (1H, m), 8.28-8.20 (2H, m), 7.99-7.90 |
| | (3H, m), 7.84-7.76 (1H, m), 7.65-7.58 (1H, m), 6.66- |
| | 6.58 (2H, m), 4.53 (1H, d, J=12Hz), 4.38 (1H, d, |
| | J=17Hz), 4.26 (1H, d, $J=12Hz$), 3.55-3,10 (7H, m), 2.89 (1H, d, $J=14Hz$), 2.24 (1H, d, $J=12Hz$), |
| 58 | 1.94-1.84 (2H, m), 1.57-1.48 (2H, m) |
| <u> </u> | DMSO-d ₆ *:8.56-8.52 (1H, m), 8.22 (1H, d, J=9Hz), 8.18- |
| | 8.08 (4H, m), 7.91-7.85 (1H, m), 7.70-7.64 (1H, m), |
| | 6 74-6 64 (3H ₂ m), 4.14-3.96 (5H ₂ m), 3.62 (1H ₂ d, |
| | J=16Hz), 3.50-3.12 (6H, m), 3.08 (1H, d, $J=12Hz$), 2.81 |
| 59 | (1H, d, J=12Hz), 1.90-1.74 (2H, m), |
| | 1.50-1.43 (2H, m), 1.19-1.13 (3H, m) |
| | CDCI ₃ *:8.40-8.33 (1H, m), 8.28-8.20 (2H, m), 8.02-7.88 |
| | (3H, m), 7.84-7.77 (1H, m), 7.61 (1H, dd, J=2, 9Hz), |
| | 6.66-6.58 (2H, m), 4.67 (1H, d, J=11Hz), 4.37 (1H, d, |
| ٠ | J=17Hz), 4.28-4.15 (3H, m), 3.61-3.21 (7H, m), |
| 60 | 3.17(1H, d, J=12Hz), 2.97(2H, s), |
| | 2.27-1.84 (3H, m), 1.56-1.46 (2H, m), 1.30 (3H, t, |
| | J=7Hz) CDCI ₃ *:8.37 (1H, s), 8.28-8.12 (2H, m), 8.02-7.93 (3H, |
| | $(10.01)_3$ = 18.37 (1H, s), 8.26-8.12 (2H, m), 6.62 7.33 (8H, m), 7.85-7.77 (1H, m), 7.66-7.60 (1H, m), 6.66-6.58 |
| | (2H, m), 4.72 (1H, d, J=11Hz), 4.36 (1H, d, J=17Hz), |
| | 4.27 (1H, d, J=12Hz), 3.77-3.67 (4H, m), 3.56-3.17 |
| 61 | (6H, m), 2.94-2.46 (6H, m), |
| " | 2.15 (1H, d, J=11Hz), 2.00-1.70 (2H, m), 1.54-1.43 |
| | (2H, m) |
| L | \Lin m/ |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

STREET SMAN 250

| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
|---------|--|
| | DMSO- $d_6*:13.3$ (1H, brs), 8.62 (1H, s), 8.33 (1H, d, J=9Hz), 8.31-8.16 (4H, m), 7.95-7.87 (1H, m), 7.80-7.72 (1H, m), 7.19 (2H, d, J=7Hz), 4.51-4.40 (1H, m), 4.34-4.05 (2H, m), 4.05-2.20 (17H, m), 2.34 (6H, s), |
| 62 | 2.04-1.82 (2H, m), 1.66-1.46 (2H, m) |
| 63 | CDC1 ₃ *:8.40-8.35 (1H, m), 8.05-8.00 (1H, m), 8.00-7.93 (3H, m), 7.84-7.77 (1H, m), 7.63 (1H, dd, J=9, 2Hz), 6.49-6.35 (1H, m), 4.55-4.48 (1H, m), 4.42 (1H, d, J=12Hz), 4.42-4.33 (1H, m), 4.26 (1H. d. J=12Hz), 4.23-4.15 (1H, m), 4.05-3.80 (2H, m), 3.49-3.28 (3H, m), 3.19 (1H, d, J=12Hz), 2.37 (1H, d, J=12Hz), 2.13 (3H, s), 2.00-1.89 (1H, m), 1.85-1.73 (1H, m), 1.53-1.43 (2H, m) |
| 64 | CDCI ₃ :8.56 (1H, s), 8.40 (1H, s), 8.20-8.15 (1H, m), 8.08-7.93 (3H, m), 7.81-7.63 (3H, m), 6.50-6.44 (1H, m), 4.55-4.15 (3H, m), 4.38 (1H, d, J=17Hz), 4.26 (1H, d, J=12Hz), 3.96-3.80 (2H, m), 3.54-3.30 (2H, m), 3.38 (1H, d, J=17Hz), 3.18 (1H, d, J=12Hz), 2.36 (1H, d, J=12Hz), 2.12 (3H, s), 1.98-1.68 (2H, m), 1.52-1.43 (2H, m) |
| 65 | CDC1 ₃ *:8.56 (1H, s), 8.40-8.36 (1H, m), 8.21-8.15 (1H, m), 8.02-7.94 (3H, m), 7.83-7.77 (1H, m), 7.63 (1H, dd, J=2, 8Hz), 6.50-6.46 (1H, m), 4.51 (1H, d, J=12Hz), 4.47-4.23 (3H, m), 4.19 (1H, d, J=12Hz), 3.96-3.83 (2H, m), 3.53-3.34 (3H, m), 3.18 (1H, d, J=12Hz), 2.38 (1H, d, J=12Hz), 2.13 (3H, s), 1.98-1.88 (1H, m), 1.85-1.59 (1H, m), 1.52-1.45 (2H, m) |
| 66 | CDC1 ₃ *:8.57 (1H, s), 8.39-8.35 (1H, m), 8.28-8.12 (1H, m), 7.99-7.93 (3H, m), 7.82-7.76 (1H, m), 7.62 (1H, dd, J=2, 9Hz), 6.53-6.46 (1H, m), 4.49-4.24 (3H, m), 3.94 (1H, d, J=12Hz), 3.99-3.76 (2H, m), 3.73 (1H, d, J=12Hz), 3.69-3.55 (1H, m), 3.51-3.36 (2H, m), 3.20 (1H, d, J=12Hz), 2.34 (1H, d, J=12Hz), 1.98-1.60 (2H, m), 1.54-1.46 (2H, m) |
| 67 | CDC1 ₃ *:8.57 (1H, s), 8.38-8.34 (1H, m), 8.22-8.17 (1H, m), 7.98-7.93 (3H, m), 7.82-7.75 (1H, m), 7.65-7.60 (1H, dd, J=2, 8Hz), 6.52-6.46 (1H, m), 4.82-4.74 (1H, m), 4.37-4.24 (3H, m), 4.11 (1H, d, J=12Hz), 3.97-3.85 (2H, m), 3.60-3.32 (4H, m), 2.50 (1H, d, J=12Hz), 1.85-1.54 (4H, m), 1.36 (3H, t, J=7Hz) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN SIM 25

FIG.30

| | F1G.30 |
|-------------|---|
| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
| | $CD_3OD+CDCI_3*:8.47-8.40$ (2H, m), 8.10-7.99 (4H, m), 7.86 |
| | (1H, dd, J=2, 9Hz), 7.67-7.60 (1H, m), 6.70-6.64 (1H, |
| | m), 4.67 (1H, d, J=11Hz), 4.20 (1H, d, J=16Hz), 4.08- |
| | 3.94 (2H, m), 3.90 (1H, d, J=12Hz), 3.68-3.31 (4H, m), |
| 68 | 2.63 (1H, d, J=11Hz), |
| | 2.02-1.92 (1H, m), 1.78-1.66 (1H, m), 1.65-1.54 (2H, m) |
| | CDCI ₃ *:8.37-8.34 (1H, m), 8.28-8.22 (2H, m), 7.99-7.92 |
| | $(3H_{\text{m}})$, $7.82-7.75$ (1H. m), $7.65-7.59$ (1H, m), $6.65-$ |
| | 6.59 (2H. m). 4.35 (1H. d. J=17Hz), 4.27-4.12 (2H, m), |
| | 3.31 (1H, d, J=17Hz), 3.56-3.17 (4H, m), 3.13 (1H, d, |
| 69 | J=12Hz), 2.37 (1H, d, J=11Hz), |
| | 1.93-1.83 (2H, m), 1.64 (3H, s), 1.53-1.45 (2H, m)
 CDC ₃ *:14.49 (1H, brs), 8.36 (1H, s), 8.32-8.12 (2H, |
| | m), 8.05-7.89 (3H, m), 7.79 (1H, d, J=8Hz), 7.63 (1H, |
| | d, J=9Hz), 7.05-6.75 (2H, m), 4.35 (1H, d, J=17Hz), |
| Ĭ | $ 4.30-4.10\ (2H, m), 4.01-3.70\ (2H, m), 3.70-3.52\ (1H, m)$ |
| 70 | m), 3.52-3.33 (1H, m), |
| | 3.33 (1H, d, J=17Hz), 3.25-3.12 (1H, m), 2.85 (3H, s), 2.48-2.35 (1H, m), 2.02-1.80 (2H, m), 1.72-1.49 (2H, |
| | m), 1.66 (3H, s) |
| <u> </u> | $CDCI_3*:8.39-8.33$ (1H, m), $8.29-8.21$ (2H, m), $8.00-7.90$ |
| | (3H. m), 7.83-7.76 (1H, m), 7.65-7.58 (1H, m), 6.66- |
| | 6.59 (2H, m), $4.40-4.26$ (2H, m), 4.20 (1H, d, $J=12Hz$), |
| | 3.71 (3H, s), 3.59-3.48 (1H, m), 3.48-3.33 (2H, m), |
| 71 | 3.34 (1H, d, J=17Hz), 3.33-3.18 (1H, m),
3.13 (1H, d, J=12Hz), 2.50-2.31 (2H, m), 2.27 (1H, d, |
| | l=12Hz), 2.14-1.70 (6H, m), 1.56-1.45 (2H, m) |
| | DMSO- d_6 *:8.58 (1H, s), 8.32-7.96 (5H, m), 7.96-7.78 |
| | (1H, m), 7.74-7.60 (1H, m), 6.84-6.62 (2H, m), 4.19- |
| 72 | 3.95 (3H, m), 3.72-2.94 (6H, m), 2.63-1.00 (12H, m) |
| | CDC1 ₃ *:8.36-8.33 (1H, m), 8.26-8.21 (2H, m), 7.98-7.92 |
| | (3H. m), $7.80-7.75$ (1H, m), 7.62 (1H, dd, J=2, 9Hz), |
| 1 | 6.64-6.59 (2H, m), 4.36 (1H, d, J=17Hz), 4.27-4.17 |
| | (2H, m), $4.06-4.00$ $(1H, m)$, $3.65-3.58$ $(1H, m)$, $3.53-$ |
| 73 | 3.16 (5H, m), 3.02 (1H, d, J=12Hz), |
| | 2.46 (1H, brs), 2.29 (1H, d, J=12Hz), 1.93-1.75 (2H, m), 1.49-1.41 (2H, m) |
| | $CDC1_3*:8.35$ (1H, s), 8.28-8.18 (2H, m), 8.01-7.88 (3H, |
| | m), 7.82-7.72 (1H, m), 7.62 (1H, dd, J=2, 9Hz), 6.68- |
| | 6.58 (2H, m), 4.35 (1H, d, J=12Hz), 4.34 (1H, d, |
| | J=17Hz), 4.25-4.18 (1H, m), 4.00-3.68 (4H, m), 3.43 |
| 74 | (1H, d, J=17Hz), 3.20-3.12 (1H, m), |
| | 3.03-2.70 (2H, m), 2.42 (1H, d, J=12Hz), 2.42 (3H, s), 2.10-1.95 (1H, m), 1.84-1.66(2H, m), 1.15-1.02 (1H, m) |
| | 2.10-1.35 (111, 117, 1.04 1.00 (211, 117, 1.10 1.02 (111, 117) |
| | |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN 5 4 25

FIG.31

| | rig. 31 |
|---------|--|
| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
| | (*:300MHz)
CDC1 ₃ *:8.38-8.33 (1H, m), 8.28-8.22 (2H, m), 8.00-7.90
(3H, m), 7.82-7.74 (1H, m), 7.65-7.58 (1H, m), 6.65- |
| 75 | 6.55 (2H, m), 4.38-4.15 (3H, m), 3.97-3.87 (1H, m), 3.83-3.72 (1H, m), 3.75 (1H, d, J=10Hz), 3.67 (1H, d, |
| | 1 1 1 1 1 1 1 1 1 |
| | 3. 34 (1H, d, J=17Hz), 3. 22 (1H, d, J=11Hz), 2. 87-2. 66 (2H, m), 2. 37 (3H, s), 2. 26 (1H, d, J=11Hz), 1. 98-1. 81 (2H, m), 1. 77-1. 58 (1H, m), 1. 15-1. 05 (1H, m) |
| | $ CD_3OD*:8.56-8.52 (1H, m), 8.18-8.06 (5H, m), 7.91 (1H,$ |
| | dd, J=2, 9Hz), 7.66 (1H, dd, J=2, 9Hz), 7.18-7.12 (2H, m), 4.51 (1H, d, J=12Hz), 4.43-4.28 (3H, m), 4.26-4.15 |
| | (1H, m), 3.89-3.75 (2H, m), 3.50 (1H, d, J=16Hz), 3.39 |
| 76 | (3H, s), 3.56-3.11 (3H, m),
2.77-2.66 (1H, m), 2.68 (6H, s), 2.61 (3H, s), 2.15- |
| | 2.02 (2H, m), 1.93-1.77 (1H, m), 1.50-1.40 (1H, m) |
| | $CDC1_3 \pm : 8.38 - 8.32$ (1H, m), 8.28-8.20 (2H, m), 8.00-7.90 (3H, m), 7.82-7.75 (1H, m), 7.61 (1H, dd, J=2, 9Hz), |
| | 6.63-6.56 (2H, m), 4.35 (1H, d, J=17Hz), 4.23-4.12 |
| 77 | (2H, m), 3.73 (1H, d, J=10Hz), 3.48 (1H, d, J=10Hz), 3.53-3.13 (5H, m), 3.44 (3H, s), |
| 77 | 2.97 (1H, d, J=12Hz), 2.52-2.44 (1H, brs), 2.24 (1H, |
| | d_{\star} J=12Hz), 1.91-1.69 (2H, m), 1.47-1.30 (2H, m) |
| | $CDCI_3*:8.37-8.32$ (1H, m), $8.31-8.24$ (2H, m), $8.00-7.90$ (3H, m), $7.81-7.74$ (1H, m), 7.61 (1H, d, $J=2$, 9Hz), |
| | le_67-6.60 (2H. m), 5.15 (1H, d, J=13Hz), 4.67 (1H, d, |
| | J=11Hz), 4.45 (1H, d, J=17Hz), 4.34 (1H, d, J=10Hz), |
| 78 | 4.00-3.77 (2H, m), 3.89 (1H, d, J=10Hz),
3.51-3.28 (2H, m), 3.36 (3H, s), 3.05-2.90 (1H, m), |
| | 2.85-2.71 (1H, m), 2.55-2.38 (1H, m), 2.32 (1H, d, |
| ł. | J=13Hz, 2.20-1.95 (2H, m), 2.10 (3H, s), 1.41-1.22 |
| | (1H, m)
 CDCl ₃ *8.40-8.35 (1H, m), 8.28-8.20 (2H, m), 8.07-7.93 |
| | (3H, m), 7.81-7.63 (3H, m), 6.65-6.57 (2H, m), 4.36 |
| 79 | (1H + 1 + 1 + 17Hz), $(2H - 4 + 14 + 14 + 14 + 14 + 14 + 14 + 14$ |
| | J=9Hz), 3.53-3.13 (6H, m), 3.45 (3H, s), 2.97 (1H, d, J=12Hz), 2.51-2.44 (1H, brs), |
| | 2.24 (1H, d, J=12Hz), 1.92-1.68 (2H, m), 1.47-1.28 |
| | (2H, m)
CDCl ₃ *:8.40-8.34 (1H, m), 8.28-8.21 (2H, m), 8.07-7.92 |
| | (3H, m), 7.79-7.62 (3H, m), 6.66-6.57 (2H, m), 4.34 |
| 80 | (1H, d, J=17Hz), 4.28-4.14 (2H, m), 3.97-3.87 (1H, m), |
| | 3.83-3.65 (3H, m), 3.38 (3H, s), 3.35 (1H, d, J=17Hz), |
| | 3.21 (1H, d, J=11Hz),
2.88-2.67 (2H, m), 2.37 (3H, s), 2.24 (1H, d, J=12Hz), |
| | 1.98-1.80 (2H, m), 1.77-1.62 (1H, m), 1.15-1.05 (1H, |
| | m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

SIM 25

FIG.32

| Ex. No. | NMR (270MHz) (ppm)
(*:300MHz) |
|---------|---|
| | CDC1 ₃ *:8.40-8.36 (1H, m), 8.28-8.20 (2H, m), 8.07-7.92 |
| | (3H, m), 7.81-7.60 (3H, m), 6.64-6.58 (2H, m), 4.43- |
| | 4.32 (2H, m), 4.20 (1H, d, J=12Hz), 3.72-3.60 (2H, m), |
| | 3.50-3.17 (5H, m), 3.44 (3H, s), 3.35 (1H, d, J=17Hz), |
| 81 | 2.28 (1H, d, J=12Hz), |
| | 2.03-1.78 (2H, m), 1.54-1.46 (2H, m) |
| | $CDCl_3*:8.40-8.36$ (1H, m), 8.28-8.20 (2H, m), 8.06-7.92 |
| | (3H, m), 7.79-7.64 (3H, m), 6.64-6.57 (2H, m), 4.43- |
| | 4.30 (2H. m), 4.20 (1H, d, J=12Hz), 3.68 (1H, d, |
| · | J=10Hz), 3.63 (1H, d, $J=10Hz$), 3.49-3.17 (5H, m), 3.44 |
| 82 | (3H. s). 3.35 (1H. d, J=17Hz), |
| | 2.28 (1H, d, J=12Hz), 2.03-1.79 (2H, m), 1.53-1.45 |
| | (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN SIA 25

| Ex. No. | NMR(ppm) (*:300MH- 270MH-) |
|--------------|--|
| 201 | (*:300MHz, 270MHz)
CDCl ₃ *:8.30-8.23 (2H, m), 7.37-7.18 (3H, m), 7.07-6.88 (2H, m), |
| | 6.70-6.63 (2H, m), 5.21-5.15 (1H, m), 4.94-4.82 (2H, m), 4.31-4.20 |
| | (2H, m), 3.84 (1H, d, J=12Hz), 3.66 (1H, d, J=17Hz), 3.67–3.52 |
| | (2H, m), 3.43–3.25 (2H, m), 3.22 (1H, d, |
| | J=12Hz), 2.89-2.80 (1H, m), 2.01-1.91 (1H, m), 1.89-1.70 (3H, m) |
| <u> </u> | CDCl ₃ *:8.32-8.24 (2H, m), 7.30 (1H, s), 7.17-7.11 (1H, m), 7.04- |
| 202 | 6.91 (2H, m), 6.70-6.63 (2H, m), 5.22-5.15 (1H, m), 4.95-4.82 (2H, |
| 202 | m), 4.32-4.18 (2H, m), 3.85 (1H, d, J=12Hz), 3.65 (1H, d, J=17Hz), |
| | 3.65-3.53 (2H, m), 3.43-3.18 (3H, m), |
| | 2.90-2.80 (1H, m), 2.02-1.91 (1H, m), 1.89-1.70 (3H, m) |
| | CDCl ₃ *:8.29-8.24 (2H, m), 7.96-7.86 (3H, m), 7.58-7.48 (2H, m), |
| 209 | 6.69-6.64 (2H, m), 5.23 (1H, d, J=4, 9Hz), 4.42-4.30 (2H, m), 3.78 |
| | (1H, d, J=12Hz), 3.65-3.48 (2H, m), 3.47 (1H, d, J=17Hz), 3.45-
3.16 (3H, m), 2.56 (1H, dd, J=9, 12Hz), 2.01- |
| | 1.92 (1H, m), 1.85-1.62 (3H, m) |
| | CDCl ₃ *:8.30-8.24 (2H, m), 7.87-7.81 (1H, m), 7.83 (1H, s), 7.62- |
| | 7.56 (1H, m), 7.36–7.28 (1H, m), 6.68–6.63 (2H, m), 5.26–5.19 (1H, |
| 210 | m), 4.41-4.29 (2H, m), 3.78 (1H, d, J=12Hz), 3.63-3.49 (2H, m), |
| | 3.48 (1H, d, J=17Hz), 3.43-3.24 (2H, m), |
| | 3.20 (1H, d, J=12Hz), 2.62-2.52 (1H, m), 2.00-1.90 (1H, m), 1.84- |
| _ | 1.62 (3H, m) |
| | $CDCl_3*:8.30-8.24$ (2H, m), $7.93-7.90$ (1H, m), $7.85-7.79$ (2H, m), |
| 211 | 7.54-7.48 (1H, m), 6.69-6.63 (2H, m). 5.22 (1H, dd, J=4, 9Hz), |
| | 4.41-4.28 (2H, m), 3.82-3.75 (1H, m), 3.64-3.48 (2H, m), 3.47 (1H, |
| | d, J=17Hz), 3.43-3.24 (2H, m), 3.24-3.18 (1H, |
| | m), 2.57 (1H, dd, J=9, 12Hz), 2.00-1.91 (1H, m), 1.84-1.63 (3H, m) |
| | CDCl ₃ *:8.30-8.24 (2H, m), 7.90-7.88 (1H, m), 7.86 (1H, d, J=9Hz), |
| 213 | 7.85-7.83 (1H, m), 7.48 (1H, dd, J=2, 9Hz), 6.69-6.64 (2H, m), |
| | 5.26-5.19 (1H, m), 4.41-4.29 (2H, m), 3.78 (1H, d, J=12Hz), 3.64- |
| | 3.50 (2H, m), 3, .47 (1H, d, J=17Hz), 3.43- |
| | 3.24 (2H, m), 3.21 (1H, d, J=12Hz), 2.62-2.52 (1H, m), 2.01-1.91 (1H, m), 1.85-1.64 (3H, m) |
| | CDCl ₃ *:8.30-8.24 (2H, m), 7.94 (1H, d, J=6Hz), 7.80 (1H, s), 7.67 |
| 219 | (1H, d, J=9Hz), 6.70-6.63 (2H, m), 5.26-5.19 (1H, m), 4.42-4.28 |
| | (2H, m), 3.83-3.75 (1H, m), 3.64-3.48 (2H, m), 3.47 (1H, d, |
| | J=17Hz), 3.43-3.24 (2H, m), 3.24-3.17 (1H, m), |
| | 2.63-2.52 (1H, m),2.01-1.90 (1H, m), 1.86-1.55 (3H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS SUBCLASS SUBCLASS

| Ex. No. | NMR(ppm)
(*:300MHz, 270MHz) |
|---------|---|
| 220 | CDCl ₃ *:8.30-8.25 (2H, m), 7.86-7.82 (1H, m), 7.78 (1H, d, J=9Hz), |
| | 7.54-7.48 (1H, m), 6.79-6.73 (2H, m), 5.25-5.17 (1H, m), 4.45-4.33 |
| | (2H, m), 3.79 (1H, d, J=12Hz), 3.64–3.47 (2H, m), 3.52 (1H, d, |
| | J=17Hz), 3.44-3.17 (3H, m), 2.72 (3H, s), |
| | 2.70-2.60 (1H, m), 2.01-1.93 (1H, m), 1.85-1.65 (3H, m) |
| | CDCl ₃ *:8.31-8.24 (2H, m), 7.72-7.68 (1H, m), 7.54-7.45 (2H, m), |
| 000 | 7.41-7.39 (1H, m), 6.69-6.64 (2H, m), 5.22-5.15 (1H, m), 4.48-4.34 |
| 223 | (2H, m), 3.80 (1H, d, J=12Hz), 3.67 (1H, d, J=17Hz), 3.64-3.51 |
| | (2H, m), 3.43-3.25 (2H, m), 3.20 (1H, d, |
| | J=12Hz), 2.82-2.72 (1H, m), 1.99-1.89 (1H, m), 1.87-1.66 (3H, m) |
| | CDCl ₃ *:8.30-8.25 (2H, m), 7.86 (1H, d, J=2Hz), 7.62 (1H, dd, J=2, |
| 224 | 9Hz), 7.46 (1H, d, J=9Hz), 7.41-7.38 (1H, m), 6.69-6.63 (2H, m), |
| 227 | 5.22-5.13 (1H, m), 4.48-4.40 (1H, m), 4.38 (1H, d, J=17Hz), 3.80 |
| 1 | (1H, d, J=12Hz), 3.67 (1H, d, J=17Hz), 3.65- |
| | 3.50 (2H, m), 3.43-3.15 (3H, m), 2.82-2.72 (1H, m), 1.98-1.88 (1H, |
| | m), 1.86-1.66 (3H, m)
CDCl ₃ *:8.30-8.24 (2H, m), 7.90-7.82 (3H, m), 7.48 (1H, dd, J=2, |
| | 9Hz), 6.68-6.63 (2H, m), 4.83-4.72 (1H, m), 4.37-4.28 (1H, m), |
| 275 | 4.31 (1H, d, J=17Hz), 3.59 (1H, d, J=12Hz), 3.47 (1H, d, J=17Hz), |
| | 3.55-3.33 (4H, m), 3.22 (1H, d, J=12Hz), |
| | 2.53-2.43 (1H, m), 1.85-1.55 (5H, m) |
| | CDCl ₃ *:8.30-8.23 (2H, m), 7.73-7.68 (1H, m), 7.53-7.44 (2H, m), |
| 005 | 7.39 (1H, s), 6.70-6.63 (2H, m), 4.78-4.67 (1H, m), 4.45-4.32 (2H, |
| 285 | m), 3.70-3.57 (2H, m), 3.55-3.32 (4H, m), 3.22 (1H, d, J=12Hz), |
| | 2.74-2.63 (1H, m), 1.85-1.57 (5H, m) |
| | CDCl ₃ *:8.31-8.25 (2H, m), 7.90-7.82 (3H, m), 7.47 (1H, dd, J=2, |
| 337 | 9Hz), 6.70-6.63 (2H, m), 4.37-4.18 (3H, m), 4.05-3.87 (2H, m), |
| "" | 3.73 (1H, d, J=12Hz), 3.48 (1H, d, J=17Hz), 3.40 (1H, d, J=12Hz), |
| | 2.95-2.72 (2H, m), 2.45 (1H, dd, J=9, |
| | 11Hz), 2.30 (3H, s), 2.00-1.87 (1H, m), 1.86-1.73 (1H, m), 1.58- |
| | 1.49 (1H, m), 1.47-1.37 (1H, m)
CDCl ₃ *:8.29 (2H, dd, J=1, 5Hz), 7.72-7.68 (1H, m), 7.53-7.43 (2H, |
| | m), 7.39 (1H, d, J=1Hz), 6.67 (2H, dd, J=2, 5Hz), 4.40-4.20 (3H, |
| 347 | m), 4.05–3.88 (2H, m), 3.77–3.70 (1H, m), 3.66 (1H, d, J=17Hz), |
| | 3.46-3.39 (1H, m), 2.95-2.73 (2H, m), |
| 1 | 2.64 (1H, dd, J=9, 11Hz), 2.30 (3H, s), 2.01-1.88 (1H, m), 1.86- |
| | 1.73 (1H, m), 1.57-1.39 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

SIL 25

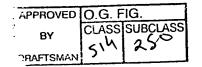
| Ex. No. | NMR(ppm)
(*:300MHz, 270MHz) |
|----------|--|
| 388 | CDCl ₃ *:8.30-8.22 (2H, m), 7.28 (1H, s), 7.16-7.11 (1H, m), 7.03- |
| | 6.97 (1H, m), 6.95–6.90 (1H, m), 6.68–6.62 (2H, m), 4.96–4.82 (2H, |
| | m), 4.32–4.18 (3H, m), 3.69 (1H, d, J=17Hz), 3.65–3.30 (6H, m), |
| | 3.41 (3H, s), 3.23 (1H, d, J=12Hz), 2.74 |
| | (1H, d, J=12Hz), 2.05-1.82 (2H, m), 1.73-1.57 (2H, m) |
| | CDCl ₃ *:8.29-8.22 (2H, m), 7.90 (1H, d, J=2Hz), 7.88-7.84 (1H, m), |
| | 7.84 (1H, s), 7.51–7.45 (1H, m), 6.66–6.60 (2H, m), 4.39–4.30 (2H, |
| 399 | m), 4.23 (1H, d, J=12Hz), 3.69-3.60 (2H, m), 3.50 (1H, d, J=17Hz), |
| | 3.50-3.26 (4H, m), 3.44 (3H, s), 3.23 |
| | (1H, d, J=12Hz), 2.43 (1H, d, J=12Hz), 2.05-1.82 (2H, m), 1.60- |
| | 1.50 (2H, m) |
| | CDCl ₃ *:8.30-8.22 (2H, m), 7.73-7.69 (1H, m), 7.56-7.45 (2H, m), |
| 400 | 7.40 (1H, s), 6.67-6.61 (2H, m), 4.45-4.34 (2H, m), 4.25 (1H, d, |
| 409 | J=11Hz), 3.73 (1H, d, J=17Hz), 3.63 (1H, d, J=10Hz), 3.59 (1H, d, |
| | J=10Hz), 3.41 (3H, s), 3.52-3.20 (5H, m), |
| | 2.63 (1H, d, J=12Hz), 2.05-1.82 (2H, m), 1.64-1.55 (2H, m) |
| | CDCl ₃ *:8.24 (2H, d, J=6Hz), 7.92-7.82 (3H, m), 7.51-7.45 (1H, m), |
| 461 | 6.62 (2H, d, J=6Hz), 4.33 (1H, d, J=17Hz), 4.21 (1H, d, J=12Hz), |
| 1 401 | 4.16 (1H, d, J=12Hz), 3.74-3.68 (1H, m), 3.55-3.18 (6H, m), 3.45 |
| | (3H, s), 2.99 (1H, d, J=12Hz), 2.49 (1H, |
| | s), 2.38 (1H, d, J=12Hz), 1.92-1.70 (2H, m), 1.50-1.40 (2H, m) |
| | CDCl ₃ *:8.28-8.23 (2H, m), 7.73-7.69 (1H, m), 7.55-7.45 (2H, m), |
| 471 | 7.40-7.38 (1H, m), 6.67-6.60 (2H, m), 4.43-4.34 (1H, m), 4.27-4.20 |
| | (1H, m), 4.21 (1H, d, J=12Hz), 3.74–3.66 (1H, m), 3.67 (1H, d, |
| | J=10Hz), 3.50-3.20 (4H, m), 3.45 (1H, d, |
| | J=10Hz), 3.42 (3H, s), 3.05-2.97 (1H, m), 2.57 (1H, d, J=12Hz), 2.49 (1H, s), 1.93-1.71 (2H, m), 1.55-1.44 (2H, m) |
| <u> </u> | CDCl ₃ *:8.27-8.23 (2H, m), 7.90-7.82 (3H, m), 7.50-7.45 (1H, m), |
| | 6.66-6.61 (2H, m), 4.37-4.28 (1H, m), 4.26-4.17 (2H, m), 3.98-3.63 |
| 523 | (4H, m), 3.54–3.45 (1H, m), 3.38 (3H, s), 3.26–3.20 (1H, m), 2.89– |
| | 2.69 (2H, m), 2.43-2.36 (1H, m), 2.38 (3H, s), |
| | 1.99-1.66 (3H, m), 1.20-1.11 (1H, m) |
| | CDCl ₃ *:8.28-8.23 (2H, m), 7.72-7.68 (1H, m), 7.54-7.44 (2H, m), |
| | 7.39-7.37 (1H, m), 6.67-6.62 (2H, m), 4.42-4.33 (1H, m), 4.29-4.21 |
| 533 | (1H, m), 4.26 (1H, d, J=12Hz), 3.98-3.77 (2H, m), 3.75-3.68 (1H, |
| | m), 3.71 (1H, d, J=10Hz), 3.60 (1H, d, |
| | J=10Hz), 3.35 (3H, s), 3.27-3.21 (1H, m), 2.91-2.69 (2H, m), 2.58 |
| | (1H, d, J=12Hz), 2.38 (3H, s), 1.99-1.69 (3H, m), 1.23-1.16 (1H, m) |
| | |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

DRAFTSMAN SIN 25

| Ex. No. | NMR(ppm)
(*:300MHz, 270MHz) |
|---------|---|
| 574 | CDCl ₃ *:8.30-8.25 (2H, m), 7.67-7.58 (2H, m), 7.46-7.36 (2H, m), |
| | 6.70-6.65 (2H, m), 5.24-5.16 (1H, m), 4.50-4.37 (1H, m), 4.37 (1H, |
| | d, J=17Hz), 3.81 (1H, d, J=12Hz), 3.70-3.51 (3H, m), 3.45-3.25 |
| | (2H, m), 3.20 (1H, d, J=12Hz), 2.82-2.73 (1H, |
| | m), 1.99-1.90 (1H, m), 1.87-1.65 (3H, m) |
| | CDCl ₃ *:9.55 (1H, brs), 8.28 (2H, d, J=5Hz), 7.73 (1H, d, J=8Hz), |
| 580 | 7.48 (1H, d, J=8Hz), 7.45-7.37 (1H, m), 7.32-7.21 (1H, m), 7.13 |
| 300 | (1H, s), 6.66 (2H, d, J=5Hz), 5.20-5.12 (1H, m), 4.36-4.26 (2H, m), |
| | 3.76 (1H, d, J=11Hz), 3.64-3.48 (2H, |
| | m), 3.43 (1H, d, J=17Hz), 3.42-3.12 (3H, m), 2.54-2.44 (1H, m), |
| | 1.98-1.86 (1H, m), 1.82-1.60 (3H, m) |
| | CDCl ₃ *:8.30-8.25 (2H, m), 7.54-7.47 (1H, m), 7.13-7.10 (1H, m), |
| 600 | 6.95-6.92 (1H, m), 6.70-6.65 (2H, m), 6.36-6.28 (1H, m), 5.19 (1H, |
| | dd, J=4, 9Hz), 4.30-4.18 (2H, m), 3.84 (1H, d, J=12Hz), 3.64-3.53 |
| | (2H, m), 3.58 (1H, d, J=17Hz), 3.44-3.27
(2H, m), 3.22 (1H, d, J=12Hz), 2.73 (1H, dd, J=9, 12Hz), 2.01-1.92 |
| | (2H, m), 3.22 (1H, d, 3-12H2), 2.73 (1H, dd, 3-9, 12H2), 2.01-1.92
(1H, m), 1.89-1.70 (3H, m) |
| | CDCl ₃ *:8.30-8.24 (2H, m), 7.54-7.45 (1H, m), 7.14-7.09 (1H, m), |
| | 6.96-6.90 (1H, m), 6.70-6.63 (2H, m), 6.37-6.28 (1H, m), 4.80-4.66 |
| 628 | (1H, m), 4.27–4.15 (2H, m), 3.64 (1H, d, J=12Hz), 3.58 (1H, d, |
| | J=17Hz), 3.56-3.35 (4H, m), 3.25 (1H, d, |
| | J=12Hz), 2.68-2.58 (1H, m), 1.90-1.60 (5H, m) |
| | CDCl ₃ *:8.32-8.25 (2H, m), 7.49 (1H, d, J=15Hz), 7.13-7.09 (1H, |
| 656 | m), 6.96-6.91 (1H, m), 6.71-6.65 (2H, m), 6.31 (1H, d, J=15Hz), |
| 000 | 4.29-4.10 (3H, m), 4.05-3.90 (2H, m), 3.79-3.71 (1H, m), 3.59 (1H, |
| | d, J=17Hz), 3.52-3.43 (1H, m), 2.97-2.75 |
| | (2H, m), 2.58 (1H, dd, J=9, 12Hz), 2.29 (3H, s), 2.02-1.89 (1H, m), |
| <u></u> | 1.87-1.73 (1H, m), 1.71-1.42 (2H, m) |
| | CDCl ₃ *:8.30-8.23 (2H, m), 7.50 (1H, d, J=15Hz), 7.14-7.10 (1H, m), 6.96-6.92 (1H, m), 6.69-6.62 (2H, m), 6.31 (1H, d, J=15Hz), |
| 684 | M), 6.96-6.92 (1H, M), 6.69-6.62 (2H, M), 6.31 (1H, d, J=15Hz),
 4.30-4.18 (3H, m), 3.67-3.56 (3H, m), 3.52-3.30 (4H, m), 3.43 (3H, |
| • | s), 3.24 (1H, d, J=12Hz), 2.62 (1H, d, |
| | J=12Hz), 2.05-1.83 (2H, m), 1.68-1.60 (2H, m) |
| | CDCl ₃ *:8.30-8.23 (2H, m), 7.48 (1H, d, J=15Hz), 7.11 (1H, d, |
| | J=4Hz), 6.93 (1H, d, J=4Hz), 6.69-6.62 (2H, m), 6.31 (1H, d, |
| 712 | J=15Hz), 4.25 (1H, d, J=12Hz), 4.22 (1H, d, J=17Hz), 4.07-4.01 |
| | (1H, m), 3.68 (1H, d, J=10Hz), 3.56 (1H, d, J=17Hz), |
| | 3.52-3.25 (4H, m), 3.47 (1H, d, J=10Hz), 3.43 (3H, s), 3.01(1H, d, |
| | J=12Hz), 2.58-2.52 (1H, m), 2.48 (1H, s), 1.95-1.72 (2H, m), 1.57- |
| | 1.50 (2H, m) |



| Ex. No. | NMR(ppm) |
|-------------|--|
| | (*:300MHz, 270MHz)
CDCl ₃ *:8.29-8.24 (2H, m), 7.52-7.45 (1H, m), 7.11 (1H, d, J=4Hz), |
| | 6.93 (1H, d, J=4Hz), 6.68-6.64 (2H, m), 6.33-6.26 (1H, m), 4.32- |
| 740 | 4.17 (2H, m), 4.14-4.08 (1H, m), 3.99-3.81 (2H, m), 3.71 (1H, d, |
| | J=10Hz), 3.66-3.56 (1H, m), 3.62 (1H, |
| | d, J=10Hz), 3.38 (3H, s), 3.27-3.21 (1H, m), 2.95-2.71 (2H, m), |
| | 2.58-2.53 (1H, m), 2.37 (3H, s), 2.01-1.73 (3H, m), 1.30-1.21 (1H, |
| | m) |
| | CDCl ₃ *:8.41-8.36 (1H, m), 8.27 (2H, dd, J=1, 5Hz), 8.06-7.93 (3H, |
| | m), 7.80-7.64 (3H, m), 6.65 (2H, dd, J=1, 5Hz), 5.24-5.17 (1H, m), |
| 759 | 4.43-4.30 (2H, m), 3.75 (1H, d, J=12Hz), 3.62-3.47 (2H, m), 3.43- |
| | 3.21 (2H, m), 3.31 (1H, d, J=17Hz), 3.18 |
| | (1H, d, J=12Hz), 2.48-2.38 (1H, m), 1.99-1.90 (1H, m), 1.82-1.60 |
| | (3H, m) |
| | CDCl ₃ *:8.40-8.36 (1H, m), 8.30-8.24 (3H, m), 8.24-8.18 (1H, m), |
| 760 | 8.06-8.01 (1H, m), 7.58 (1H, d, J=9Hz), 6.69-6.63 (2H, m), 5.24- |
| 760 | 5.17 (1H, m), 4.44-4.29 (2H, m), 3.80-3.73 (1H, m), 3.63-3.48 (2H, |
| | m), 3.42-3.23 (2H, m), 3.33 (1H, d, J=17Hz), |
| | 3.22-3.16 (1H, m), 2.54-2.45 (1H, m), 2.00-1.90 (1H, m), 1.84-1.58 |
| | (3H, m) |
| | CDCl ₃ *:8.27 (2H, d, J=6Hz), 7.87 (1H, s), 7.66-7.60 (1H, m), 7.56- |
| 761 | 7.50 (1H, m), 7.43 (1H, s), 6.67 (2H, d, J=6Hz), 5.23-5.15 (1H, m), |
| '0' | 4.50-4.33 (2H, m), 3.80 (1H, d, J=12Hz), 3.67 (1H, d, J=17Hz), |
| | 3.66-3.50 (2H, m), 3.45-3.24 (2H, m), 3.20 |
| | (1H, d, J=12Hz), 3.12 (1H, s), 2.83-2.72 (1H, m), 2.00-1.67 (4H, m) |
| | CDCl ₃ *:8.38-8.34 (1H, m), 8.27 (2H, dd, J=2, 5Hz), 7.99-7.90 (3H, |
| 765 | m), 7.82-7.76 (1H, m), 7.65-7.59 (1H, m), 6.65 (2H, dd, J=2, 5Hz), |
| /03 | 4.80-4.69 (1H, m), 4.40-4.32 (1H, m), 4.32 (1H, d, J=16Hz), 3.59- |
| | 3.28 (6H, m), 3.20 (1H, d, J=12Hz), 2.40-2.30 |
| | (1H, m), 1.85-1.50 (5H, m) |
| | CDCl ₃ *:8.38-8.33 (1H, m), 8.31-8.24 (2H, m), 7.98-7.89 (3H, m), |
| 769 | 7.81-7.76 (1H, m), 7.63-7.58 (1H, m), 6.70-6.62 (2H, m), 4.36-4.22 |
| | (3H, m), 4.04-3.85 (2H, m), 3.70 (1H, d, J=11Hz), 3.40-3.27 (2H, |
| } | m), 2.94–2.70 (2H, m), 2.37–2.25 (1H, m), |
| | 2.30 (3H, s), 1.99-1.73 (2H, m), 1.65-1.49 (1H, m), 1.44-1.34 (1H, |
| | m)
 CDCl₃*:8.39-8.35 (1H, m), 8.29-8.19 (4H, m), 8.05-8.00 (1H, m), |
| | 7.59 (1H, d, J=9Hz), 6.64-6.59 (2H, m), 4.41-4.32 (2H, m), 4.21 |
| 770 | (1H, d, J=12Hz), 3.69-3.58 (2H, m), 3.49-3.18 (5H, m), 3.43 (3H, |
| | s), 3.37 (1H, d, J=17Hz), 2.34 (1H, d, J=12Hz), |
| | |
| L | 2.03-1.81 (2H, m), 1.55-1.49 (2H, m) |

APPROVED O.G. FIG.

BY CLASS SUBCLASS

SIM 250

FIG.38

| | NMR(ppm) |
|---------|---|
| Ex. No. | (*:300MHz, 270MHz) |
| | DMSO-d ₆ *:13.25 (1H, s), 8.59 (1H, s), 8.28-8.17 (4H, m), 8.14- |
| | |
| 776 | 8.08 (1H, m), 7.88 (1H, dd, J=2, 9Hz), 7.80-7.68 (2H, m), 7.23 (2H, |
| | d, J=7Hz), 5.25-5.18 (1H, m), 4.23-4.14 (1H, m), 4.06 (1H, d, |
| | J=17Hz), 4.00-3.81 (2H, m), 3.71 (1H, d, |
| | J=12Hz), 3.62-3.35 (3H, m), 3.15 (1H, d, J=12Hz), 2.75-2.65 (1H, |
| | m), 2.31 (3H, s), 2.00–1.52 (4H, m) |
| | DMSO-d ₆ *:13.22 (1H, s), 8.39-8.34 (1H, m), 8.25-8.15 (3H, m), |
| 777 | 8.12-8.07 (1H, m), 7.63-7.57 (1H, m), 7.19 (2H, d, J=7Hz), 4.18- |
| ''' | 4.02 (3H, m), 3.92-3.28 (7H, m), 3.33 (3H, s), 3.20 (1H, d, J=12Hz), |
| | 2.82 (1H, d, J=11Hz), 2.30 (3H, s), |
| | 1.94-1.78 (2H, m), 1.70-1.48 (2H, m) |
| | DMSO-d ₆ *:13.23 (1H, s), 8.26-8.18 (2H, m), 7.65-7.57 (1H, m), |
| 778 | 7.52 (1H, d, J=4Hz), 7.26-7.19 (3H, m), 7.09-7.02 (1H, m), 4.24- |
| '' | 4.17 (1H, m), 4.01-3.74 (5H, m), 3.62-3.47 (4H, m), 3.32 (3H, s), |
| | 3.26-3.20 (1H, m), 2.90-2.84 (1H, m), 2.30 (3H, |
| | s), 1.93-1.83 (2H, m), 1.71-1.60 (2H, m) |
| | DMSO-d ₆ *:13.23 (1H, s), 8.28-8.15 (2H, m), 7.99-7.72 (3H, m), |
| 779 | 7.67-7.57 (1H, m), 7.28-7.14 (2H, m), 4.23-4.03 (3H, m), 3.93-3.71 |
| 779 | (3H, m), 3.67-3.15 (5H, m), 3.32 (3H, s), 3.07-2.97 (1H, m), 2.30 |
| | (3H, s), 1.98-1.77 (2H, m), 1.70-1.53 (2H, m) |
| | DMSO-d ₆ *:13.23 (1H, s), 8.27-8.18 (2H, m), 7.52-7.46 (1H, m), |
| 700 | 7.50 (1H, s), 7.26-7.20 (2H, m), 7.12 (1H, dd, J=2, 8Hz), 7.08-7.06 |
| 780 | (1H, m), 5.02 (2H, s), 4.20 (1H, d, J=12Hz), 4.05-3.75 (5H, m), |
| | 3.65-3.45 (4H, m), 3.31 (3H, s), 3.23 (1H, d, |
| | J=12Hz), 3.03 (1H, d, J=11Hz), 2.29 (3H, s), 2.00-1.55 (4H, m) |

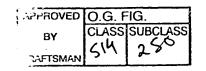


FIG.39

<TABLE A>

COORDINATES OF THE ACTIVE CENTER SITES IN THE CRYSTAL STRUCTURE OF COMPOUND A - FXA COMPLEX ARE SHOWN BELOW IN PDB FORMAT

| WWW. WWW. WWW. WWW. WWW. WWW. WWW. WWW | 4586788901234567888888888888888888888888888888888888 | ① YYYYYYYYYYYYYYYYYYYYYYYYYYYYYYYYYYYY | 966666666667777777778888888899999999999 | \$\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | 10. 293
11. 268
10. 872
9. 3882
9. 3892
7. 5044
6. 736
6. 920
7. 047
10. 849
11. 119
9. 8498
7. 943
7. 350
12. 1860
12. 1861
11. 363
12. 486
12. 496
13. 691
14. 112
13. 691
14. 113
14. 116
15. 828
15. 828
15. 839
16. 828
17. 709
18. 692
19. 758
19. 758
1 | ® 448
10.3129.3454
8.2399.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
9.2818
10.2818
11.2855
11.2855
12.187
12.187
12.187
12.187
12.187
13.888
14.844
15.857
16.638
17.229
16.638
17.229
16.638
17.229
18.899
19.818
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
10.918
1 | 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 | 48. 48
41. 77
19. 85
21. 36
20. 12
25. 14
26. 75
19. 21
20. 00
17. 75
18. 62
17. 99
14. 90
15. 82
17. 93
18. 63
17. 93
18. 63
18. 63 |
|--|--|--|---|---|--|--|---|--|
|--|--|--|---|---|--|--|---|--|

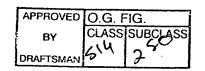
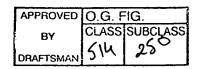


FIG.40

CONTINUED FROM (TABLE A)

| ATOM | 1587 | 7 C | PHE | 174 | -4.654 | 19.705 | 11.000 | 1. | 00 | 16.38 |
|--------|------|------|-------|-----|--------|---------|---------|------|-----|-------|
| ATOM | 1588 | | PHE | | -4.788 | | | | 00 | 20.64 |
| MOTA | 1745 | | ASP | 189 | 8. 408 | | | | .00 | 12.09 |
| | | | | | 9. 304 | | | | 00 | 0.00 |
| MOTA | 1746 | | ASP | 189 | | | | | | |
| ATOM | 1747 | | | 189 | 8.045 | | | | 00 | 14.13 |
| ATOM | 1748 | | ASP | 189 | 7.060 | | | | 00 | 18.27 |
| ATOM | 1749 | | ASP | 189 | 6.299 | | 10.447 | | 00 | 29.21 |
| ATOM | 1750 | 00 | 1 ASP | 189 | 6.899 | | | | 00 | 26.93 |
| MOTA | 1751 | 00 | 2 ASP | 189 | 5.077 | | 10.152 | | 00 | 28.08 |
| ATOM | 1752 | C | ASP | 189 | 9.333 | | 11.053 | 1. | 00 | 14.52 |
| ATOM | 1753 | 0 | ASP | 189 | 10.370 | 32.219 | 10.606 | 1. | 00 | 17.15 |
| ATOM | 1754 | N | ALA | 190 | 9.301 | 30.508 | 11.571 | 1. | 00 | 10.01 |
| ATOM | 1755 | н | ALA | 190 | 8.522 | 30.238 | 12.091 | 1. | 00 | 0.00 |
| ATOM | 1756 | CA | ALA | 190 | 10.453 | 29.820 | 11.470 | ١. | 00 | 5.72 |
| ATOM | 1757 | | ALA | 190 | 10.325 | 28.473 | 12.450 | 1. | 00 | 9.56 |
| ATOM | 1758 | С | ALA | 190 | 10.396 | 29.112 | 10.025 | 1. | 00 | 5.82 |
| ATOM | 1759 | 0 | ALA | 190 | 9.799 | 29.761 | 9. 186 | 1. | 00 | 9.42 |
| ATOM | 1760 | N | CYS | 191 | 10.988 | 27.960 | 9.728 | 1. | 00 | 3.41 |
| ATOM | 1761 | Н | CYS | 191 | 11.414 | 27.439 | 10.437 | 1. | 00 | 0.00 |
| ATOM | 1762 | CA | CYS | 191 | 10.979 | 27.440 | 8.360 | 1. | 00 | 6.67 |
| ATOM | 1763 | С | CYS | 191 | 11.864 | 26.196 | 8, 255 | 1. | 00 | 5.52 |
| ATOM | 1764 | 0 | CYS | 191 | 12.375 | 25.715 | 9.277 | 1. | 00 | 6.15 |
| ATOM | 1765 | C8 | CYS | 191 | 11.469 | 28.518 | 7.387 | 1. | 00 | 8.63 |
| ATOM | 1766 | SG | CYS | 191 | 11.102 | 28.223 | 5.629 | 1. | 00 | 18.50 |
| MOTA | 1767 | N | GLN | 192 | 12.098 | | . 7.033 | 1. | 00 | 5.87 |
| ATOM | 1768 | Н | GLN | 192 | 11.679 | 26.167 | 6.270 | 1.1 | 00 | 0.00 |
| ATOM | 1769 | CA | GLN | 192 | 12.925 | 24.515 | 6.820 | 1.0 | 00 | 10.96 |
| MOTA | 1770 | CB | GLN | 192 | 13.086 | 24.254 | 5.331 | 1.0 | 00 | 17.72 |
| ATOM | 1771 | CG | GLN | 192 | 13.700 | 22.910 | 5.018 | 1.0 | | 32.49 |
| ATOM | 1772 | CD | GLN | 192 | 14.143 | 22.802 | 3.575 | 1.0 | 0(| 41.58 |
| ATOM | 1773 | 0ET | GLN | 192 | 15.327 | 22.950 | 3.264 | 1.0 | 00 | 44.38 |
| MOTA | 1774 | NE2 | GLN | 192 | 13.194 | 22.551 | 2.678 | 1.0 | | 43.85 |
| MOTA | 1775 | HE21 | GLN | 192 | 12.259 | 22.433 | 2.903 | 1.0 | 0 | 0.00 |
| ATOM | | HE22 | | 192 | 13.527 | 22.509 | 1.763 | 1.0 | | 0.00 |
| ATOM | 1777 | С | GLN | 192 | 14.316 | 24.525 | 7.478 | 1.0 | 0 | 7.56 |
| ATOM | 1778 | 0 | GLN | 192 | 14.974 | 25. 563 | 7.548 | 1.0 | 0 | 2.44 |
| ATOM | 1779 | N | GLY | 193 | 14.761 | 23.372 | 7.964 | 1.0 | 0 | 8. 11 |
| MOTA | 1780 | Н | GLY | 193 | 14.237 | 22.555 | 7.869 | 1.0 | 0 | 0.00 |
| MOTA | 1781 | CA | GLY | 193 | 16.064 | 23.313 | 8.603 | 1.0 | 0 | 9.56 |
| MOTA | 1782 | С | GLY | 193 | 16.035 | 23.720 | 10.065 | 1.0 | 0 | 11.52 |
| MOTA | 1783 | 0 | GLY | 193 | 16.889 | 23.315 | 10.843 | 1.0 | 0 | 15.90 |
| ATOM: | 1784 | N | ASP | 194 | 15.080 | 24.571 | 10.431 | 1.0 | 0 . | 12.53 |
| MOTA | 1785 | Н | ASP | 194 | 14.493 | 24.947 | 9.749 | 1.0 | 0 | 0.00 |
| MOTA | 1786 | CA | ASP | 194 | 14.915 | 24.987 | 11.814 | 1.0 | 0 | 7.55 |
| MOTA | 1787 | CB | ASP | 194 | 13.908 | 26.131 | 11.915 | 1.0 | 0 | 2.00 |
| MOTA | 1788 | CG | ASP | 194 | 14.475 | 27.465 | 11.459 | 1.0 | 0 | 2.00 |
| MOTA | 1789 | OD 1 | ASP | 194 | 13.728 | 28. 235 | 10.814 | 1.0 | 0 | 4.12 |
| ATOM | 1790 | 0D2 | ASP | 194 | 15.651 | 27.765 | 11.761 | 1.0 | 0 | 7.76 |
| ATOM | 1791 | С | ASP | 194 | 14.402 | 23.791 | 12.621 | 1.0 | Ó | 9.73 |
| ATOM | 1792 | 0 | ASP | 194 | 14.536 | 23.750 | 13.840 | 1.0 | | 2.71 |
| ATOM | 1793 | Ň | SER | 195 | 13.804 | 22.823 | 11.938 | 1.0 | | 6.99 |
| MOTA | 1794 | H | SER | 195 | 13.748 | 22.953 | 10.974 | 1.0 | | 0.00 |
| MOTA | 1795 | CA | SER | 195 | 13.264 | 21.625 | 12.589 | 1.0 | | 0.57 |
| ATOM | 1796 | CB | SER | 195 | 12.968 | 20. 532 | 11.555 | 1.0 | | |
| | | OG | | 195 | 11.748 | | | | | 0.36 |
| MOTA | 1797 | | SER | | | 20.787 | 10.868 | 1.00 | | 8.45 |
| MOTA | 1798 | HC | SER | 195 | 11.756 | 21.696 | 10.548 | 1.00 | | 0.00 |
| MOTA | 1799 | | SER | 195 | 14.136 | 21.054 | 13.707 | 1.00 | | 8.30 |
| MOTA | 1800 | | SER | 195 | 15.298 | 20.752 | 13.486 | 1.00 | | 3.26 |
| A-T OM | 1965 | | VAL | 213 | 10.619 | 22.878 | 17.479 | 1.00 | | 8.87 |
| MOTA | 1966 | Н | VAL | 213 | 11.529 | 23.087 | 17.805 | 1.00 | | 0.00 |
| | | | | | | | | | | - |



CONTINUED FROM (TABLE A)

| TATATATATATATATATATATATATATATATATATATA | 19689
1977
1977
1977
1977
1977
1977
1977
19 | 0E2
C 0 N H CA
C 0 N H CA
C 0 O | LLLLLLARRERERERERERERERERERERERERERERERE | 217
217
217
218
218
218
218
218
218
220
220
220
220
220 | 10.3614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
213614
2 | 20. 536
20. 731
21. 3491
19. 618
19. 1885
20. 751
19. 1885
21. 317
23. 787
23. 787
23. 787
24. 238
25. 766
25. 359
26. 859
27. 469
27. 525
28. 859
29. 599
21. 710
21. 710
22. 25. 766
25. 369
27. 27. 27. 27. 27. 27. 27. 27. 27. 27. | 11. 450
11. 174
12. 230
10. 133
12. 617
13. 914
12. 285
10. 258
11. 259
10. 258
10. | 1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00 | 3. 61
4. 20
2. 000
5. 71
2. 004
6. 05
10. 05
10. 05
11. 54
11. 75
12. 40
12. 40
12. 40
12. 40
13. 81
14. 80
15. 81
16. 83
17. 70
16. 84
17. 20
17. 20
18. 81
19. 61
10. 66
11. 54
11. 6. 68
11. 6. 68
12. 16
15. 30
16. 54
17. 20
17. 20
18. 81
19. 61
10. 61
10. 61
11. 54
11. 6. 62
12. 16
15. 58
10. 05
10. 05
11. 54
11. 6. 66
12. 30
13. 55
14. 81
15. 58
16. 66
17. 20
18. 81
19. 61
10. 61
10. 66
11. 52
12. 16
13. 81
14. 84
15. 84
16. 66
17. 20
17. 20
18. 81
19. 61
10. 61 |
|--|---|--|--|--|--|---|--|--|--|
| MOTA
MOTA | 2019
2020 | CA
C
CB
SG
N | CYS
CYS | 220
220 | 6.833
6.352 | 29.599
31.034 | 5.838
5.783 | 1.00
1.00 | 9.17
13.52
15.23 |

| APPROVED | O.G. FIG. | | | | | | |
|-----------|-----------|----------|--|--|--|--|--|
| BY | CLASS | SUBCLASS | | | | | |
| DRAFTSMAN | 617 | 20 | | | | | |

CONTINUED FROM (TABLE A)

| 00. | | 、、、、、、 | ,22,70 |
|--|---|---|--------|
| MMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMM | 2096 O GL
 2097 N IL
 2098 H IL
 2099 CA IL
 2100 CB IL
 2101 CG2 IL
 2102 CG1 IL
 2103 CD1 IL
 2104 C IL
 2105 O IL
 2106 N TY | YEE E E E E E E E E E E E E E E E E E E | 3.728 |

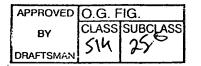
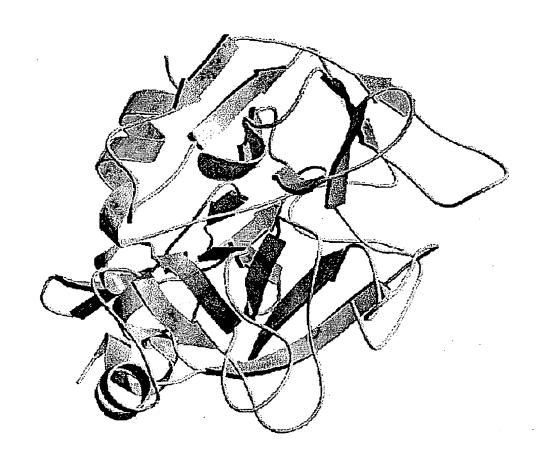


FIG.43



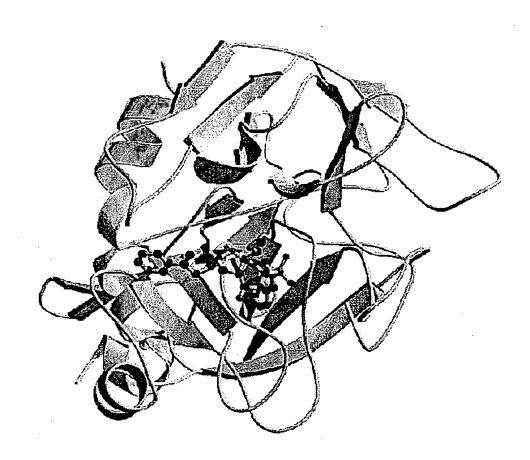
Human Factor Xa (Des-Gla domain)

APPROVED O.G. FIG.

BY CLASS SUBCLASS

SIM 250

FIG.44



Human Factor Xa (Des-Gla domain)—Compound A

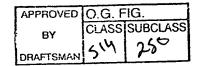
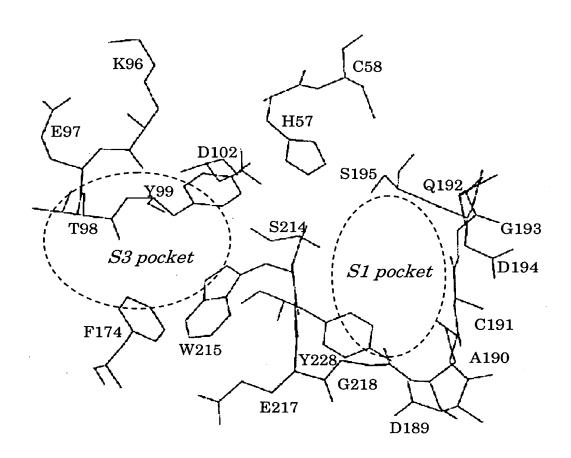


FIG.45



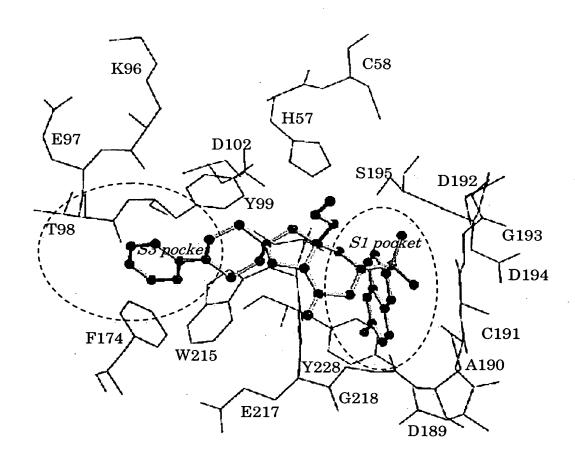
Factor Xa Active Site

APPROVED O.G. FIG.

BY CLASS SUBCLASS

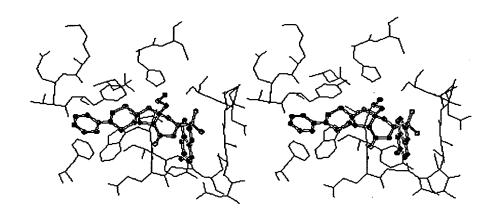
DRAFTSMAN SIM 25

FIG. 46



Factor Xa Active Site occupied Compound A





Stereo View Factor Xa Active Site occupied Compound A





- ①CHYMOTRYPSIN NO. IN 1FAX STRUCTURE
- ②AMINO ACID SEQUENCE OF THE SERINE PROTEASE DOMAIN IN FXA

③SERIAL NO. OF THE RESIDUES OF THE SERINE PROTEASE DOMAIN IN FXA

| DO | MAIN | IIN | FXA | | | | | _ | _ | | | • | <u> </u> | 3 |
|------|-------|-----|------------|------------|----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| ① | 2 | 3 | ① | 2 | ③ | ① | @ | 3 | ① | 2 | 3 | ① | ②
CYS | 209 |
| 16 | ILE | 1 | 67 | ARG | 53 | 119 | ALA | 105 | 169 | LYS | 157 | 220 | ALA | 210 |
| 17 | VAL | 2 | 68 | VAL | 54 | 120 | PRO | 106 | 170 | LEU | 158 | 221 | ARG | 211 |
| 18 | GLY | 3 | 69 | GLY | 55 | 121 | ALA | 107 | 171 | SER | 159 | 222 | | |
| 19 | GLY | 4 | 70 | ASP | 56 | 122 | CYS | 108 | 172 | SER | 160 | 223 | LYS | 212
213 |
| 20 | GLN | 5 | 71 | ARG | 57 | 123 | LEU | 109 | | SER | 161 | 223A | GLY | |
| 21 | GLU | 6 | 72 | ASN | 58 | 124 | PRO | 110 | 174 | PHE | 162 | 224 | LYS | 214 |
| 22 | CYS | 7 | 73 | THR | 59 | 124A | GLU | 111 | 175 | ILE | 163 | 225 | TYR | 215 |
| 23 | LYS | 8 | 74 | ALA | 60 | | ARG | 112 | 176 | ILE | 164 | 226 | GLY | 216 |
| 24 | ASP | 9 | 75 | ALA | 61 | 126 | ASP | 113 | 177 | THR | 165 | 227 | ILE | 217
218 |
| 25 | GLY | 10 | 76 | GLU | 62 | 127 | TRP | 114 | 178 | GLN | 166 | 228 | TYR | 219 |
| 26 | GLU · | 11 | 77 | GLU | 63 | 128 | ALA | 115 | 179 | ASN | 167 | 229 | THR | 220 |
| 27 | CYS | 12 | 78 | GLY | 64 | 129 | GLU | 116 | 180 | MET | 168 | 230 | LYS
VAL | 221 |
| 28 | PRO | 13 | 79 | GLY | 65 | 130 | SER | 117 | 181 | PHE | 169 | 231
232 | THR | 222 |
| 29 | TRP | 14 | 80 | GLU | 66 | 131 | THR | 118 | 182 | CYS | 170 | 232 | ALA | 223 |
| 30 | GLN | 15 | 81 | ALA | 67 | 131A | Ά | 119 | 183 | ALA | 171 | 234 | PHE | 224 |
| 31 | ALA | 16 | 82 | VAL | 68 | 131B | MET | 120 | 184 | GLY | 172
173 | 235 | LEU | 225 |
| 32 | LEU | 17 | · 83 | HIS | 69 | 132 | THR | 121 | 185 | TYR | 174 | 236 | LYS | 226 |
| 33 | LΕU | 18 | 84 | GLU | 70 | 133 | GLN | 122 | 185A | ASP | 175 | 237 | TRP | 227 |
| 34 | ILE | 19 | 85 | VAL | 71 | 134 | LYS | 123 | 185B | THR
LYS | 176 | 238 | ILE | 228 |
| 35 | ASN | 20 | 86 | GLU | 72 | 135 | THR | 124 | 186
187 | GLN | 177 | 239 | ASP | 229 |
| 36 | GLU | 21 | 87 | VAL | 73 | 136 | GLY | 125 | | GLU | 178 | 240 | ARG | 230 |
| 37 | GLU | 22 | 88 | VAL | 74 | 137 | ILE | 126 | 188
189 | ASP | 179 | 241 | SER | 231 |
| 38 | ASN | 23 | 89 | ILE | 75 | 138 | VAL | 127 | 190 | ALA | 180 | 242 | MET | 232 |
| 39 | GLU | 24 | 90 | LYS | 76 | 139 | SER | 128
129 | 191 | CYS | 181 | 243 | LYS | 233 |
| 40 | GLY | 25 | 91 | HIS | 77 | 140 | GLY | 130 | 192 | GLN | 182 | 244 | THR | 234 |
| 41 | PHE | 26 | 92 | ASN | 78 | 141 | PHE
GLY | 131 | 193 | GLY | 183 | | | |
| 42 | CYS | 27 | - | ARG | 79 | 142
143 | ARG | 132 | 194 | ASP | 184 | | | |
| 43 | GLY | 28 | | PHE | 80 | 144 | THR | 133 | 195 | SER | 185 | | | |
| 44 | GLY | 29 | 95 | THR | 81 | 145 | HIS | 134 | 196 | GLY | 186 | | | |
| 45 | THR | 30 | 96 | LYS | 82 | 147 | GLU | 135 | 197 | GLY | 187 | | | |
| 46 | ILE | 31 | 97 | GLU | 83 | 148 | LYS | 136 | 198 | PRO | 188 | | | |
| 47 | LEU | 32 | 98 | THR | 84
85 | 149 | GLY | 137 | 199 | HIS | 189 | | | |
| 48 | SER | 33 | 99 | TYR | 86 | 150 | ARG | 138 | 200 | VAL | 190 | | | |
| 49 | GLU | 34 | 100 | ASP
PHE | 87 | 151 | GLN | 139 | 201 | THR | 191 | | | |
| 50 | PHE | 35 | 101 | ASP | 88 | 152 | SER | 140 | 202 | ARG | 192 | | | |
| 51 | TYR | 36 | 102 | ILE | 89 | 153 | THR | 141 | 203 | PHE | 193 | | | |
| 52 | ILE | 37 | 103 | ALA | 90 | | ARG | 142 | 204 | LYS | 194 | | | |
| 53 | LEU | 38 | 104
105 | VAL | 91 | 155 | LEU | 143 | 205 | ASP | 195 | | | |
| 54 | THR | 39 | | LEU | 92 | 156 | LYS | 144 | 206 | THR | 196 | | | |
| 55 | ALA | 40 | 106 | | 93 | 157 | MET | 145 | 207 | TYR | 197 | | | |
| 56 | ALA | 41 | | ARG | 94 | 158 | LEU | 146 | 208 | PHE | 198 | | | |
| 57 | HIS | 42 | 108 | LEU | 95 | 159 | GLU | 147 | 209 | VAL | 199 | | | |
| 58 | CYS | 43 | 109 | LYS | 96 | 160 | VAL | 148 | 210 | THR | 200 | | | |
| 59 | LEU | 44 | | THR | 97 | | PRO | 149 | 211 | GLY | | | | |
| 60 | TYR | 45 | | PRO | | | TYR | 150 | 212 | ILE | 202 | | | |
| 61 | GLN | 46 | 112 | ILE | 98 | | VAL | 151 | 213 | VAL | 203 | | | |
| 61 A | | 47 | 113 | THR | 99 | 163 | ASP | 152 | 214 | SER | 204 | | | |
| 62 | LYS | 48 | | PHE | 100 | | | 153 | 215 | TRP | 205 | | | |
| | ARG | 49 | | ARG | 101 | | ARG | | | GLY | 205 | | | |
| 64 | PHE | 50 | | MET | 102 | | ASN | 154 | 218 | | 207 | | | |
| 65 | LYS | 51 | | ASN | 103 | 167 | SER | 155 | 217 | GLU | | | | |
| 66 | VAL | 52 | 118 | VAL | 104 | 168 | CYS | 156 | 218 | GLY | 200 | | | |
| | | | | | | | | | | | | | | |